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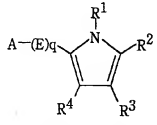
(54) PYRROLE DERIVATIVES AND MEDICINAL COMPOSITION

(57) The invention relates to a pharmaceutical composition comprising a pyrrole derivative of the following formula [1] or a pharmaceutically acceptable salt thereof, or a solvate of either of them, as an active ingredient.



[1]

(wherein R^1 represents hydrogen or alkoxycarbonylamino, R^2 represents alkyl, aryl which may be substituted, aromatic heterocyclyl which may be substituted, unsubstituted amino, monoalkylamino, dialkylamino, or cyclic amino which may be substituted; R^3 represents cyano or carbamoyl; R^4 represents hydrogen or alkyl; E represents alkylene; q is equal to 0 or 1, A represents methyl, aryl which may be substituted, or aromatic heterocyclyl which may be substituted)

The pharmaceutical composition of the invention is effective for the treatment of pollakiuria or urinary incontinence.

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Description

TECHNICAL FIELD

The present invention relates to a pyrrole derivative, a pharmaceutically acceptable salt thereof, and a solvate of either of them, all of which are useful as medicines.

The compound of the invention has urinary bladder capacity increasing activity and is useful for the treatment of pollakiuria and urinary incontinence.

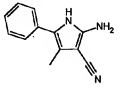
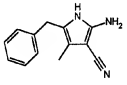
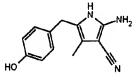
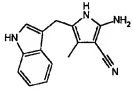
BACKGROUND ART

The frequency of urination of healthy humans is generally 4-6 times a day and usually no urine is voided during sleep at night. The condition of an abnormally increased frequency of urination is called pollakiuria and the condition of involuntary emptying of the urinary bladder is known as urinary incontinence. Both morbidities are bothersome to the affected person because sleep is disturbed and going out is restricted. The frequency of occuring pollakiuria or urinary incontinence is particularly high in the bedridden aged persons and patients with dementia and there is a pressing need for development of useful therapeutic drug in this field, not only for patients and clinical doctors but also for the people taking charge of nursing care.

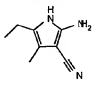
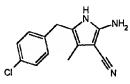
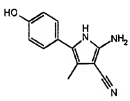
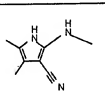
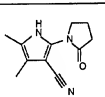
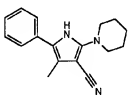
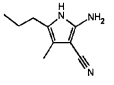
As therapeutic drugs designed to ameliorate pollakiuria and urinary incontinence through increase in bladder capacity, flavoxate, oxybutynin, propiverine and so on are used today.

Meanwhile, as pyrrole derivatives apparently resembling the compound of the present invention, the compounds listed below in Table 1 are known. However, none of them are known to have the first medicinal use, namely, to be useful for the treatment of disease such as pollakiuria or urinary incontinence.

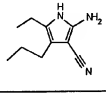
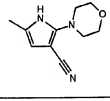
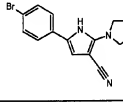
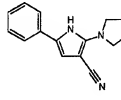
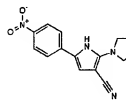
Table 1

Compound No.	Structural formula	Literature
R1		J. Prakt. Chem., 318, 663 (1976).
R2		J. Heterocyclic Chem., 14, 383 (1977). Z. Chem., 1, 349 (1961).
R3		J. Heterocyclic Chem., 14, 383 (1977).
R4		J. Heterocyclic Chem., 14, 383 (1977).
R5		Khim. Geterotsiki. Soedim., (9), 1217, (1975) (Chem. Abstr., 84, 59299 (1976))
R6		J. Heterocyclic Chem., 14, 383 (1977).

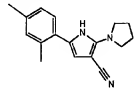
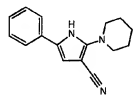
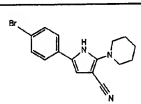
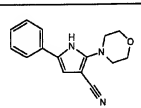
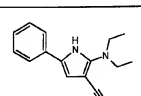
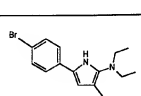
Continuation of Table 1

R7		Khim. Geterotsiki. Soedim., (9), 1217, (1975) (Chem. Abstr., 84, 59299 (1976))
R8		J. Pharm. Sci., 68, 317 (1979).
R9		Synthesis, 217 (1979).
R10		Synthesis, 55 (1974).
R11		J. Pharm. Sci., 65, 908 (1976). J. Heterocyclic Chem., 23, 397 (1986).
R12		Farmaco, Ed. Sc., 43, 103 (1988).
R13		Khim. Geterotsiki. Soedim., (9), 1217, (1975) (Chem. Abstr., 84, 59299 (1976))

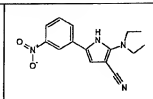
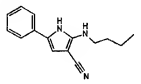
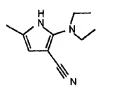
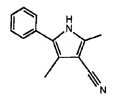
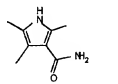
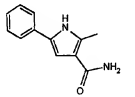
Continuation of Table 1

R14		J. Heterocyclic Chem., 14, 383 (1977).
R15		Khim. Geterotsiki. Soedim., (9), 1217, (1975) (Chem. Abstr., 84, 59299 (1976))
R16		Farmaco, Ed. Sc., 43, 103 (1988).
R17		Farmaco, Ed. Sc., 43, 103 (1988).
R18		Farmaco, Ed. Sc., 43, 103 (1988).
R19		Farmaco, Ed. Sc., 43, 103 (1988).

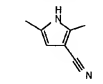
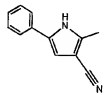
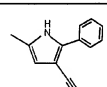
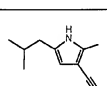
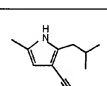
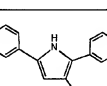
Continuation of Table 1

R20		Farmaco, Ed. Sc., 43, 103 (1988).
R21		Farmaco, Ed. Sc., 43, 103 (1988).
R22		Farmaco, Ed. Sc., 43, 103 (1988).
R23		Farmaco, Ed. Sc., 43, 103 (1988).
R24		Farmaco, Ed. Sc., 43, 103 (1988).
R25		Farmaco, Ed. Sc., 43, 103 (1988).

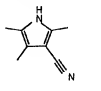
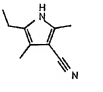
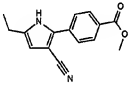
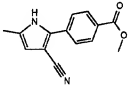
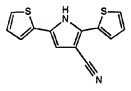
Continuation of Table 1

R26		Farmaco, Ed. Sc., 43, 103 (1988).
R27		Farmaco, Ed. Sc., 43, 103 (1988).
R28		Farmaco, Ed. Sc., 43, 103 (1988).
R29		J. Chem. Res., Synop. (8), 266 (1992). J. Chem. Res., Miniprint, 2049 (1992).
R30		Heterocycles, 10, 261 (1978).
R31		Heterocycles, 10, 261 (1978).

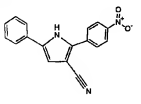
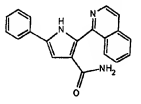
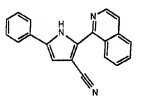
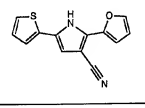
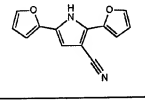
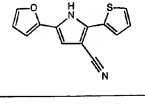
Continuation of Table 1

R32		J. Org. Chem., 43, 4273 (1978). J. Chem. Soc., B, (1), 79 (1970).
R33		J. Org. Chem., 43, 4273 (1978).
R34		J. Org. Chem., 43, 4273 (1978). EP 358047 A2.
R35		J. Org. Chem., 43, 4273 (1978).
R36		J. Org. Chem., 43, 4273 (1978).
R37		J. Org. Chem., 43, 4273 (1978). Heterocycles, 20, 829 (1983).

Continuation of Table 1

R38		J. Chem. Soc., B, (1), 79 (1970).
R39		Gazz. Chim. Ital., 71, 375 (1941).
R40		Justus Liebigs Ann. Chem., 447, 43 (1926).
R41		WO 93/19067.
R42		EP 480204 A1.
R43		EP 314009 A2. EP 389904 A2.

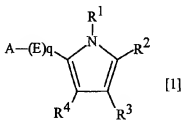
Continuation of Table 1

R44		Chem. Ber., 105, 1258 (1972).
R45		J. Org. Chem., 31, 4110 (1996).
R46		J. Org. Chem., 31, 4110 (1996).
R47		EP 389904 A2.
R48		EP 389904 A2.
R49		EP 389904 A2.

DISCLOSURE OF INVENTION

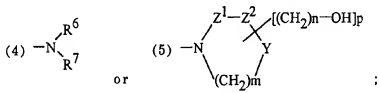
The inventors of the present invention did much research for developing a drug which is structurally different from the hitherto-known therapeutic drugs for pollakiuria or urinary incontinence and is more useful than those drugs.

As a result, the inventors found that the pyrrole derivative of the following formula [1] or a pharmaceutically acceptable salt thereof, or a solvate of either of them, has excellent bladder capacity increasing activity and is useful as a therapeutic drug for pollakiuria or urinary incontinence. The present invention has been completed on the basis of the above finding.



[1]

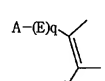
wherein R^1 represents hydrogen or alkoxycarbonylamino:
R^2 represents (1) alkyl, (2) aryl which may be substituted, (3) aromatic heterocyclyl which may be substituted,



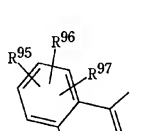
;

R^6 and R^7 may be the same or different and each represents (1) hydrogen or (2) alkyl (which alkyl may be substituted by (1) hydroxy, (2) aryl which may be substituted by alkoxy, or (3) aromatic heterocyclyl);
Z^1 and Z^2 may be the same or different and each represents $-CH_2-$ or >C=O; provided that Z^1 and Z^2 do not concurrently represent >C=O;
Y represents $-CH_2-$, -O-, -S-, or $>NR^9$;
R^9 represents hydrogen, alkyl, acyl, aryl, or aromatic heterocyclyl;
m represents an integer of 1-3; n represents an integer of 0-2; p represents 0 or 1;
in case R^2 represents aryl which may be substituted or aromatic heterocyclyl which may be substituted, the aryl or aromatic heterocyclyl may be substituted by 1 member or 2-3 different members selected from the group consisting of (1) halogen, (2) alkyl which may be substituted by halogen, (3) cyano, (4) nitro, (5) alkoxycarbonyl, (6) hydroxy, (7) alkoxy (which alkoxy may be substituted by halogen, aryl which may be substituted by alkoxy, or alkoxy), (8) $-NHSO_2R^{82}$, and (9) $-NR^{83}R^{84}$; or two adjacent substituent groups may jointly represent $-O-(CH_2)_t-O-$,
R^{82} represents (1) alkyl or (2) aryl which may be substituted by alkyl;
t represents 1 or 2;
R^{83} and R^{84} may be the same or different and each represents (1) hydrogen, (2) alkyl, or (3) acyl; or R^{83} and R^{84} jointly and taken together with the adjacent N atom represent 5-through 7-membered cyclic amino;
R^3 represents cyano or carbamoyl;
R^4 represents hydrogen or alkyl;
E represents alkylene; q represents 0 or 1;
A represents (1) methyl, (2) aryl which may be substituted, or (3) aromatic heterocyclyl which may be substituted;
in case A represents aryl which may be substituted or aromatic heterocyclyl which may be substituted, the aryl or aromatic heterocyclyl may be substituted by 1 member or 2-3 different members selected from the group consisting of (1) halogen, (2) alkyl which may be substituted by halogen, (3) cyano, (4) nitro, (5) alkoxycarbonyl, (6) hydroxy, (7) alkoxy (which alkoxy may be substituted by halogen, aryl which may be substituted by alkoxy, or alkoxy), (8) $-NHSO_2R^{92}$, and (9) $-NR^{93}R^{94}$; or two adjacent substituent groups may jointly represent $-O-(CH_2)_u-O-$;
R^{92} represents (1) alkyl or (2) aryl which may be substituted by alkyl;
u represents 1 or 2;
R^{93} and R^{94} may be the same or different and each represents (1) hydrogen, (2) alkyl, or (3) acyl; or R^{93} and R^{94}

jointly and taken together with the adjacent N atom represent 5-through 7-membered cyclic amino, A-(E)q, R^4, and the double bond of the pyrrole ring may jointly, i.e. as



represent



;

X represents -O-, -S-, or >NR^{90} where R^{90} represents alkyl;

R^{95}, R^{96} and R^{97} may be the same or different and each is selected from the group consisting of (1) hydrogen, (2) halogen, (3) alkyl which may be substituted by halogen, (4) cyano, (5) nitro, (6) alkoxycarbonyl, (7) hydroxy, (8) alkoxy (which alkoxy may be substituted by halogen or alkoxy), (9) -$NHSO_2R^{92}$ (R^{92} is as defined above), and (10) -$NR^{93}R^{94}$ (R^{93} and R^{94} are as defined above); any two adjacent substituent groups among R^{95}, R^{96}, and R^{97} may jointly represent -O-$(CH_2)_u$-O- (u is as defined above).

The present invention relates to a pharmaceutical composition comprising the compound of formula [1] as an active ingredient. The present invention further relates to the compound of formula [1].

Depending on the combination of specific substituent groups, the compound of formula [1] includes known compounds. However, it was discovered for the first time by the inventors of the present invention that those known compounds have bladder capacity increasing activity.

Thus, among pyrrole derivatives of formula [1], the following compounds (1)-(28) are known compounds, while the other compounds are novel compounds not described in any literature.

(1) the compound in which R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is methyl, q is equal to 0, and A is methyl, phenyl, or 4-hydroxyphenyl,

(2) the compound in which R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is methyl, -(E)q- is -CH_2-, and A is methyl, phenyl, 4-hydroxyphenyl, 4-chlorophenyl, or 3-indolyl,

(3) the compound in which R^1 is hydrogen, R^2 is morpholino, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is methyl or phenyl,

(4) the compound in which R^1 is hydrogen, R^2 is 1-pyrrolidinyl, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is phenyl, 4-bromophenyl, 4-nitrophenyl, or 2,4-dimethylphenyl,

(5) the compound in which R^1 is hydrogen, R^2 is 1-piperidinyl, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is phenyl or 4-bromophenyl,

(6) the compound in which R^1 is hydrogen, R^2 is diethylamino, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is methyl, phenyl, 4-bromophenyl, or 3-nitrophenyl,

(7) the compound in which R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is methyl, -(E)q- is -CH_2CH_2-, and A is methyl,

(8) the compound in which R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is n-propyl, -(E)q- is -CH_2-, and A is methyl,

(9) the compound in which R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is methyl, -(E)q- is -$CH(CH_3)CH_2$-, and A is

methyl,

(10) the compound in which R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is ethyl, q is equal to 0, and A is methyl,

(11) the compound in which R^1 is hydrogen, R^2 is methylamino, R^3 is cyano, R^4 is methyl, q is equal to 0, and A is methyl,

(12) the compound in which R^1 is hydrogen, R^2 is 2-oxopyrrolidin-1-yl, R^3 is cyano, R^4 is methyl, q is equal to 0, and A is methyl,

(13) the compound in which R^1 is hydrogen, R^2 is 1-piperidinyl, R^3 is cyano, R^4 is methyl, q is equal to 0, and A is phenyl,

(14) the compound in which R^1 is hydrogen, R^2 is n-butylamino, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is phenyl,

(15) the compound in which R^1 is hydrogen, R^2 is methyl, R^3 is cyano, R^4 is methyl, q is equal to 0, and A is methyl or phenyl,

(16) the compound in which R^1 is hydrogen, R^2 is methyl, R^3 is carbamoyl, R^4 is methyl, q is equal to 0, and A is methyl,

(17) the compound in which R^1 is hydrogen, R^2 is methyl, R^3 is carbamoyl, R^4 is hydrogen, q is equal to 0, and A is methyl or phenyl,

(18) the compound in which R^1 is hydrogen, R^2 is methyl, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is methyl or phenyl,

(19) the compound in which R^1 is hydrogen, R^2 is methyl, R^3 is cyano, R^4 is hydrogen, -(E)q- is $-CH(CH_3)CH_2-$, and A is methyl,

(20) the compound in which R^1 is hydrogen, R^2 is phenyl, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is methyl or phenyl,

(21) the compound in which R^1 is hydrogen, R^2 is isobutyl, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is methyl,

(22) the compound in which R^1 is hydrogen, R^2 is 4-methoxycarbonylphenyl, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is methyl,

(23) the compound in which R^1 is hydrogen, R^2 is 4-methoxycarbonylphenyl, R^3 is cyano, R^4 is hydrogen, -(E)q- is $-CH_2-$, and A is methyl,

(24) the compound in which R^1 is hydrogen, R^2 is 2-thienyl, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is 2-thienyl or 2-furyl,

(25) the compound in which R^1 is hydrogen, R^2 is 4-nitrophenyl, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is phenyl,

(26) the compound in which R^1 is hydrogen, R^2 is 1-isoquinolyl, R^3 is cyano or carbamoyl, R^4 is hydrogen, q is equal to 0, and A is phenyl,

(27) the compound in which R^1 is hydrogen, R^2 is 2-furyl, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is 2-thienyl or 2-furyl,

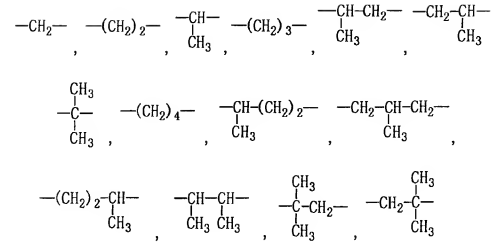
(28) the compound in which R^1 is hydrogen, R^2 is methyl, R^3 is cyano, R^4 is methyl, -(E)q- is $-CH_2-$, and A is methyl.

The alkyl in formula [1] includes straight-chain or branched alkyl group of 1-4 carbon atoms, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, or tert-butyl.

The aryl includes aryl group of 6-12 carbon atoms, such as phenyl, 1-naphthyl, 2-naphthyl, 3-biphenyl, or 4-biphenyl.

The aromatic heterocyclyl includes aromatic 5- or 6-membered heterocyclic group containing 1-4 hetero-atoms selected from among nitrogen, oxygen and sulfur, and the corresponding benzologue (benzene-fused) systems (provided that 2-pyrrolyl and 3-pyrrolyl are excluded), such as 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrimidinyl, 4-pyrimidinyl, 1-indolyl, 2-indolyl, 3-indolyl, 1-tetrazolyl, 2-furyl, 3-furyl, 2-benzofuranyl, 3-benzofuranyl, 2-thienyl, and 3-thienyl.

The alkylene includes straight-chain or branched alkylene group of 1-4 carbon atoms, such as the following.



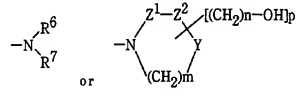
The alkyl moiety of said alkoxy, alkoxycarbonyl, or alkoxycarbonylamino includes the alkyl group mentioned above by way of example.

The halogen includes fluorine, chlorine, bromine, and iodine.

The acyl includes acyl group of 1-7 carbon atoms, such as formyl, acetyl, propionyl, butyryl, isobutyryl, valeryl, isovaleryl, pivaloyl, hexanoyl, isohexanoyl, or benzoyl.

The 5- through 7-membered cyclic amino represented by $NR^{83}R^{84}$ or $NR^{93}R^{94}$ includes 1-pyrrolidinyl, 1-piperidinyl, and 1-hexamethyleneimino, among others.

Preferred species of the compound [1] of the invention include those in which R^2 is



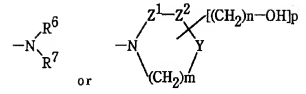
Still more preferred species of compound [1] according to the present invention are those in which R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is hydrogen or alkyl, q is equal to 0, and A is aryl which may be substituted or aromatic heterocyclyl which may be substituted.

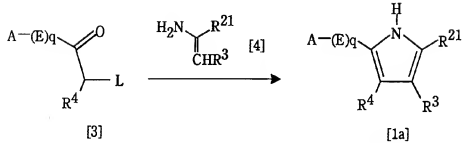
Particularly preferred species of compound [1] according to the present invention are the following compounds (1)-(6).

(1) the compound in which R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is methyl, q is equal to 0, and A is phenyl,
(2) the compound in which R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is methyl, q is equal to 0, and A is 2-fluorophenyl,
(3) the compound in which R^1 is hydrogen, R^2 is NH_2 , R^3 is cyano, R^4 is methyl, q is equal to 0, and A is 2,5-difluorophenyl,
(4) the compound in which R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is methyl, q is equal to 0, and A is 3-pyridyl,
(5) the compound in which R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is phenyl,
(6) the compound in which R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is 4-fluorophenyl,

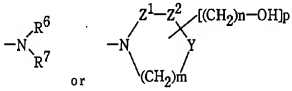
The compound [1] according to the present invention can be produced, for example, by the following processes.

Synthetic Process A (production of compound [1a] corresponding to formula [1] wherein R^1 is hydrogen and R^2 is





[In the above reaction schema, A, E, q, R^3, and R^4 are as defined hereinbefore; R^{21} represents

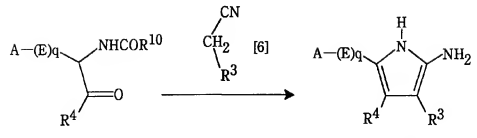


R^6, R^7, Z^1, Z^2, Y, m, n, and p are as defined hereinbefore; L represents halogen such as chlorine, bromine, or iodine]

Compound [1a] can be synthesized by reacting compound [3] with compound [4].

This reaction can be generally carried out in a solvent that does not interfere with the reaction (e.g. alcohols such as methanol, ethanol, n-propanol, isopropanol, n-butanol and tert-butanol, ethers such as tetrahydrofuran (THF) and diethyl ether, halogenated hydrocarbons such as chloroform and methylene chloride, hydrocarbons such as benzene, toluene and n-hexane, polar solvents such as acetonitrile, N,N-dimethylformamide (DMF), dimethyl sulfoxide (DMSO) and ethyl acetate and mixture of such solvents), either in the presence of a base (e.g. ammonia, sodium hydrogen carbonate, potassium hydrogen carbonate, potassium carbonate, sodium carbonate, pyridine, 4-dimethylaminopyridine, triethylamine) or in the absence of the base, at -20 to 100°C. The reaction time is dependent on the species of compound [3] and compound [4] used and the reaction temperature but may generally range from 1 minute to 24 hours. The molar ratio of compound [4] to compound [3] is generally 1-2:1. Compound [4] may be used in excess so that it may function as the base as well.

Synthesis Process B (production of compound [1b] corresponding to formula [1] wherein R^1 is hydrogen and R^2 is NH_2)



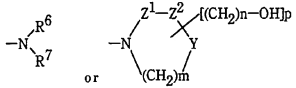
[5] [1b]

[In the above reaction schema, A, E, q, R^3, and R^4 are as defined above; R^{10} represents alkyl such as that mentioned hereinbefore]

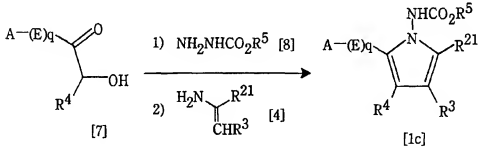
Compound [1b] can be synthesized by reacting compound [5] with compound [6].

This reaction is generally carried out in a solvent that does not interfere with the reaction (e.g. alcohols such as methanol, ethanol, n-propanol, isopropanol, n-butanol and tert-butanol, ethers such as tetrahydrofuran (THF) and diethyl ether, halogenated hydrocarbons such as chloroform and methylene chloride, hydrocarbons such as benzene, toluene and n-hexane and, polar solvents such as acetonitrile, N,N-dimethylformamide (DMF) and dimethyl sulfoxide (DMSO), and mixture of such solvents), within the pH range of 9.5-10.5 as adjusted by addition of a base (e.g. a sodium alkoxide such as sodium methoxide or sodium ethoxide, piperidine, triethylamine, 30-60% aqueous solution of sodium hydroxide, 30-60% aqueous solution of potassium hydroxide) at -10 to 100°C. The reaction time is dependent on the species of compound [5] and compound [6] and the reaction temperature but may generally range from 5 minutes to 24 hours. The molar ratio of compound [6] to compound [5] is generally 1-2:1.

Synthetic Process C (production of compound [1c] corresponding to formula [1] wherein R^1 is alkoxycarbonyl amino and R^2 is



or)



[7] [1c]

[In the above reaction schema, A, E, q, R^{21}, R^3, and R^4 are as defined hereinbefore; R^5 represents a straight-chain or branched alkyl group of 1-4 carbon atoms]

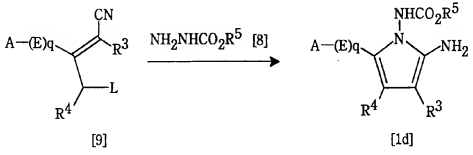
Compound [1c] can be synthesized by reacting compound [7] with compound [8] in the known manner (J. Heterocyclic Chem., 17, 1793, 1980) and subjecting the reaction product further to reaction with compound [4].

The reaction of compound [7] with compound [8] can be generally carried out in a solvent which does not interfere with the reaction (e.g. ethers such as tetrahydrofuran (THF) and diethyl ether, halogenated hydrocarbons such as chloroform and methylene chloride, hydrocarbons such as benzene, toluene and n-hexane, polar solvents such as acetonitrile, N,N-dimethylformamide (DMF) and dimethyl sulfoxide (DMSO), and mixture of such solvents), either in the presence of a catalytic amount of an acid (e.g. concentrated hydrochloric acid, zinc chloride, boron tri-

fluoride) or in the absence of the acid, at 0-150°C, while the byproduct water is continuously distilled off.

To this reaction mixture is added compound [4] at 10-30°C and the whole mixture is heated at 40-100°C. The reaction time depends on the species of compound [7], compound [8], and compound [4] used and the reaction temperature but may generally range from 30 minutes to 24 hours. The proportions of compound [8] and compound [4] are generally 1-1.2 molar equivalents based on compound [7].

Synthetic Process D (production of compound [1d] corresponding to formula [1] wherein R^1 is alkoxycarbonylamino and R^2 is NH_2)



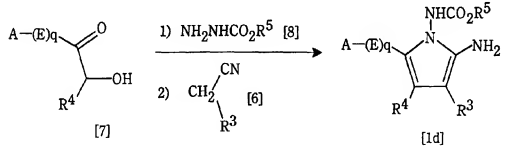
[9] [1d]

[In the above reaction schema, A, E, q, R^3, R^4, R^5, and L are as defined hereinbefore]

Compound [1d] can be synthesized by reacting compound [9] with compound [8] in the known manner (J. Prakt. Chem., 318, 663, 1976).

This reaction can be generally carried out in a solvent which does not interfere with the reaction (e.g. alcohols such as methanol, ethanol, n-propanol, isopropanol, n-butanol and tert-butanol, ethers such as tetrahydrofuran (THF) and diethyl ether, halogenated hydrocarbons such as chloroform and methylene chloride, hydrocarbons such as benzene, toluene and n-hexane, polar solvents such as acetonitrile, N,N-dimethylformamide (DMF) and dimethyl sulfoxide (DMSO), and mixture of such solvents) at 20-100°C. The reaction time is dependent on the species of compound [9] and compound [8] and the reaction temperature but may generally range from 30 minutes to 24 hours. The molar ratio of compound [8] to compound [9] is generally 1-1.2:1.

Synthetic Process E (production of compound [1d] corresponding to formula [1] wherein R^1 is alkoxycarbonylamino and R^2 is NH_2)



[7] [1d]

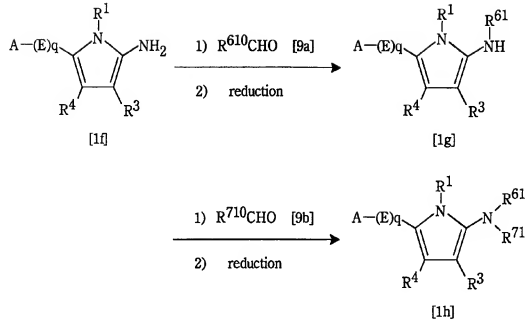
[In the above reaction schema, A, E, q, R^3, R^4, and R^5 are as defined hereinbefore]

Compound [1d] can be synthesized by reacting compound [7] with compound [8] and subjecting the reaction product further to reaction with compound [6].

Except that compound [6] is used in lieu of compound [4], the reaction can be carried out in the similar manner as in Synthetic Process C.

Starting with the compound [1f] corresponding to compound [1] of the invention wherein R^2 is NH_2, which is synthesized by the above Synthetic Processes A-E, the compound in which R^2 is alkyl-substituted amino can be synthesized by the following Synthetic Process F or Synthetic Process G.

Synthetic Process F (production of compound [1g] corresponding to formula [1] wherein R^2 is monoalkylamino and compound [1h] corresponding to formula [1] wherein R^2 is dialkylamino)



[In the above reaction schemes, A, E, q, R^1, R^3, and R^4 are as defined hereinbefore. R^{61} and R^{71} may be the same or different and each represents alkyl such as that mentioned hereinbefore (which alkyl may be substituted by (1) hydroxy, (2) aryl which may be substituted by alkoxy, or (3) aromatic heterocyclyl). R^{610} and R^{710} represent residues available upon elimination of the bonding-end $-CH_2-$ from R^{61} and R^{71}, respectively]

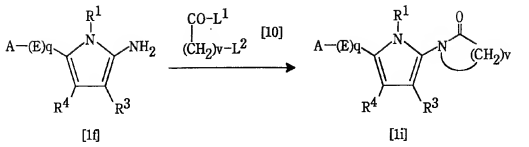
Compound [1g] can be synthesized by reacting compound [1f] with aldehyde [9a] and then reducing the reaction product. Compound [1h] can be synthesized from compound [1g] and aldehyde [9b] in the similar manner.

The reaction of compound [1f] with aldehyde [9a] can be generally carried out in the absence of a solvent or in a solvent which does not interfere with the reaction (e.g. ethers such as tetrahydrofuran (THF) and diethyl ether, halogenated hydrocarbons such as chloroform and methylene chloride, hydrocarbons such as benzene, toluene and n-hexane, polar solvents such as acetonitrile, N,N-dimethylformamide (DMF) and dimethyl sulfoxide (DMSO), and mixture of such solvents), either in the presence of a dehydrating agent (e.g. magnesium sulfate, sodium sulfate, active calcium sulfate, molecular sieves) or in the absence of the dehydrating agent, at 0-150°C. The reaction time is dependent on the species of compound [1f] and aldehyde [9a] and the reaction temperature but may generally range from 30 minutes to 120 hours. The molar ratio of aldehyde [9a] to compound [1f] is generally 1-1.2:1.

The reduction reaction can be carried out using a reducing agent such as sodium borohydride or sodium cyanoborohydride in a solvent which does not interfere with the reaction (e.g. methanol, ethanol, isopropanol, DMF, DMSO, acetonitrile, or ethyl acetate, or a mixture thereof) at -10 to 40°C. The reaction time is dependent on the species of compound [1f], aldehyde [9a], and reducing agent used and the reaction temperature but may generally range from 30 minutes to 24 hours. The proportion of the reducing agent is generally 1-10 moles per mole of compound [1f].

In carrying out this synthetic process, an orthoformic ester (e.g. methyl orthoformate, ethyl orthoformate) can be used in lieu of formaldehyde (compound [9a] (R^{610}=H), compound [9b] (R^{710}=H)).

Synthetic Process G (production of compound [1i] corresponding to formula [1] wherein R^2 is 2-oxocyclic amino (Y is $-CH_2-$))



[1f] [10] [1i]

[In the above reaction schema, A, E, q, R^1, R^3, and R^4 are as defined hereinbefore; L^1 and L^2 may be the same or different and each represents halogen such as chlorine, bromine, or iodine; v represents an integer of 3-5.

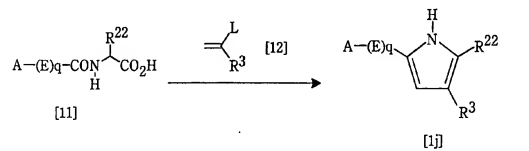
Compound [1i] can be produced by reacting compound [1f] with compound [10].

In this reaction, the acyl halide moiety of compound [10] undergoes reaction in the first place and the alkyl halide moiety then undergoes reaction.

The reaction of the acyl halide moiety can be generally carried out in a solvent which does not interfere with the reaction (e.g. ethers such as tetrahydrofuran (THF) and diethyl ether, halogenated hydrocarbons such as chloroform and methylene chloride, hydrocarbons such as benzene, toluene and n-hexane, polar solvents such as acetonitrile, N,N-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), and mixture of such solvents) in the presence of a base (e.g. sodium hydrogen carbonate, potassium hydrogen carbonate, potassium carbonate, sodium carbonate, pyridine, 4-dimethylaminopyridine, triethylamine) at -78 to 100°C. The reaction time is dependent on the species of compound [1f] and compound [10] and the reaction temperature but may generally range from 30 minutes to 24 hours. The molar ratio of compound [10] to compound [1f] is 1-1.2:1. The proportion of the base is generally 1-10 moles per mole of compound [1f].

The reaction of the alkyl halide moiety is carried out using the compound obtained in the previous step and a strong base (e.g. potassium tert-butoxide, sodium methoxide, sodium ethoxide, sodium hydride) in a solvent which does not interfere with the reaction (e.g. alcohols such as methanol and ethanol, ethers such as tetrahydrofuran (THF) and diethyl ether, halogenated hydrocarbons such as chloroform and methylene chloride, hydrocarbons such as benzene, toluene and n-hexane, polar solvents such as acetonitrile, N,N-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), and mixture of such solvents) at 0-100°C. The reaction time is dependent on the species of compound [1f] and compound [10] and the reaction temperature but may generally range from 30 minutes to 24 hours. The proportion of the strong base is generally 1-1.2 molar equivalents based on compound [1f].

Synthetic Process H (production of compound [1j] corresponding to formula [1] wherein R^1 is hydrogen, R^2 is (1) alkyl, (2) aryl which may be substituted, or (3) aromatic heterocyclyl which may be substituted, and R^4 is hydrogen)



[11] [12] [1j]

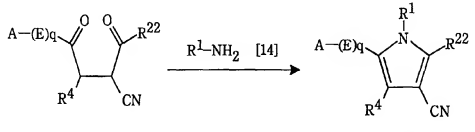
[In the above reaction schema, A, E, q, R^3, and L are as defined hereinbefore; R^{22} represents (1) alkyl such as that defined hereinbefore, (2) optionally substituted aryl such as that defined hereinbefore, or (3) optionally substituted aromatic heterocyclyl such as that defined hereinbefore]

Compound [1j] can be synthesized by reacting compound [11] with compound [12] in the presence of an acid anhydride (e.g. acetic anhydride, propionic anhydride, an anhydride of A-(E)q-CO_2H).

This reaction is generally carried out using the above-mentioned acid anhydride as a solvent at 0-160°C. The reaction time is dependent on the species of compound [11] and compound [12] and the reaction temperature but

may generally range from 5 minutes to 24 hours. The molar ratio of compound [12] to compound [11] is generally 10-20:1. The proportion of said acid anhydride is generally 10-100 moles per mole of compound [11].

Synthetic Process I (production of compound [1k] corresponding to formula [1] wherein R^2 is (1) alkyl, (2) aryl which may be substituted, or (3) aromatic heterocyclyl which may be substituted, and R^3 is cyano)



[13] [1k]

[In the above reaction schema, A, E, q, R^1, R^4, and R^{22} are as defined hereinbefore]

Compound [1k] can be synthesized by reacting compound [13] with either compound [14] or its acid addition salt.

This reaction can be generally carried out in a solvent which does not interfere with the reaction (e.g. alcohols such as methanol, ethanol, n-propanol, isopropanol, n-butanol, and tert-butanol, ethers solvent such as tetrahydrofuran (THF) and diethyl ether, halogenated hydrocarbons such as chloroform and methylene chloride, hydrocarbons such as benzene, toluene and n-hexane, polar solvents such as acetonitrile, N,N-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), and mixture of such solvents), either in the presence of an acid catalyst (e.g. acetic acid, p-toluenesulfonic acid) or in the absence of the acid, at 20-160°C. The reaction time is dependent on the species of compound [13] and compound [14] and the reaction temperature but may generally range from 5 minutes to 18 hours. The molar ratio of compound [14] to compound [13] is generally 1-5:1. The proportion of the acid catalyst is generally 0.1-2 moles per mole of compound [13]. The acid catalyst (such as acetic acid) may be used in excess so that it may function as the solvent as well.

Referring to species of compound [1] wherein R^3 is cyano, this R^3 can be converted to carbamoyl by the known procedure.

With regard to species of compound [1] wherein R^2 and A respectively represent nitro-substituted aryl or nitro-substituted aromatic heterocyclyl, the nitro can be converted to amino by the known procedure.

Compound [1] can be isolated and purified from the reaction mixture by conventional separation-purification techniques such as extraction, concentration, neutralization, filtration, recrystallization, column chromatography, thin-layer chromatography, and ion exchange chromatography as used selectively in a suitable combination.

Any species of compound [1] of the invention that is basic can be used in the form of a free base as a medicine but may be converted to a pharmaceutically acceptable salt by the per se known method and used as such. The salt includes salts with mineral acids such as hydrochloric acid, hydrobromic acid, sulfuric acid and phosphoric acid and salts with organic acids such as acetic acid, citric acid, tartaric acid, maleic acid, succinic acid, fumaric acid, p-toluenesulfonic acid, benzenesulfonic acid and methanesulfonic acid.

The hydrochloride, for instance, can be obtained by dissolving compound [1] in alcoholic hydrochloric acid.

There are cases in which a solvate (inclusive of hydrate) of the compound [1] or salt of the invention is available upon recrystallization of the solvated compound from the corresponding solvent or an appropriate solvent mixture containing the corresponding solvent. Such solvates also fall within the scope of the invention.

For instance, there is the case that the hydrate of compound [1] according to the invention is obtained upon recrystallization of compound [1] from an aqueous alcohol.

Compound [1] of the invention may show polymorphism and in such cases the respective polymorphs also fall within the scope of the invention.

The compound [3] through compound [14], which are used as starting compounds in the production of compound [1] of the invention are either known compounds or compounds which can be prepared by the similar process to per se known processes as described in Reference Examples which appear hereinafter.

The compound of the invention is useful as a medicine. As can be understood from the Test Examples presented hereinafter, the compound of the invention has potent bladder capacity increasing activity and is useful particularly as a therapeutic drug for pollakiuria or urinary incontinence.

In the administration of the compound of the invention as a medicine, the compound can be administered either as

it is or in the form of a pharmaceutical composition containing 0.1-99.5%, preferably 0.5-90%, of the compound in a pharmaceutically acceptable, nontoxic and inert carrier, to animals including humans.

The carrier includes solid, semisolid or liquid diluents, fillers and other formulation auxiliaries and they may be used either solely or jointly. The pharmaceutical composition is preferably administered in unit dosage forms. The pharmaceutical composition of the invention can be administered intravenously, orally, into the tissue, topically (e.g. transdermally), or rectally. Of course, the dosage form suited to each route of administration should be selected. Oral administration is particularly advantageous.

The dosage of the pharmaceutical composition of the invention for the treatment of pollakiuria or urinary incontience is preferably established in consideration of patient factors, e.g. age and body weight, route of administration, nature and severity of disease, etc. Usually, however, the daily dose as an effective amount of the compound of the invention for adult patients is 0.1-1000 mg/patient, preferably 1-500 mg/patient.

Lower doses may be sufficient in some cases and higher doses may be needed in other cases. The above dosage may be administered in 2-3 divided doses a day.

BEST MODE FOR CARRYING OUT THE INVENTION

The following Examples, Test Examples and Formulation Examples for the pharmaceutical composition of the invention are further illustrative of the present invention.

Reference Example 1

2-Bromo-2',5'-difluoropropiophenone

To a solution of 2',5'-difluoropropiophenone (2.12 g) in diethyl ether (20 ml) under ice-cooling was added bromine dropwise, and the mixture was stirred at room temperature overnight. To this reaction mixture was added ice and the diethyl ether layer was separated, followed by washing with water and saturated aqueous solution of sodium hydrogen carbonate in that order and dried over anhydrous magnesium sulfate ($MgSO_4$). The ether layer was concentrated under reduced pressure to provide the title compound.

The following compounds were synthesized by substantially the same procedure as Reference Example 1.

2-Bromo-4'-ethoxyacetophenone,
Bromomethyl 3-thienyl ketone,
2-Bromo-3',4'-methylenedioxyacetophenone,
2-Bromo-2',4'-difluoroacetophenone,
2-Bromo-2',5'-difluoroacetophenone,
2-(Bromoacetyl)benzofuran,
2-Bromo-4'-methanesulfonamidoacetophenone,
2-Bromoacetophenone,
2-Bromo-4'-methoxyacetophenone,
2-Bromo-4'-chloroacetophenone,
2-Bromo-4'-bromoacetophenone,
2-Bromo-4'-nitroacetophenone,
2-Bromo-4'-methylacetophenone,
2-Bromo-3'-methoxyacetophenone,
2-Bromo-2'-methoxyacetophenone,
Bromomethyl 2-thienyl ketone,
2-Bromo-3'-ethoxyacetophenone,
2-Bromo-4'-phenylacetophenone,
2-Bromo-3',4'-dichloroacetophenone,
2-Bromo-4'-fluoroacetophenone,
3-(Bromoacetyl)pyridine,
2-Bromo-4'-isopropoxyacetophenone,
2-(Bromoacetyl)naphthalene,
2-Bromo-3'-chloroacetophenone,
2-Bromo-3'-methyl-4'-chloroacetophenone,
2-(Bromoacetyl)pyridine,
Bromoacetone,
(1-Bromoethyl) methyl ketone,

2-Bromo-4'-n-propoxyacetophenone,
2-Bromo-4'-(2-methoxyethoxy)acetophenone,
2-Bromo-4'-(2-ethoxyethoxy)acetophenone,
2-Bromo-4'-benzyloxyacetophenone,
2-Bromo-2'-fluoroacetophenone,
2-Bromo-3'-fluoroacetophenone,
2-Bromo-4'-trifluoromethylacetophenone,
2-Bromo-2'-trifluoromethylacetophenone,
2-Bromo-3'-(2-methoxyethoxy)acetophenone,
2-(Bromoacetyl)furan,
2-Bromo-3'-fluoro-4'-methoxyacetophenone,
2-Bromo-2'-fluoro-4'-metoxyacetophenone,
2-Bromo-4'-(2-fluoroethoxy)acetophenone,
2-Bromo-3'-(2-fluoroethoxy)acetophenone,
2-Bromo-5'-bromo-2',4'-diethoxypropiophenone,
2-Bromo-2'-ethoxypropiophenone,
2-Bromo-4'-isopropoxypropiophenone,
2-Bromo-3',5'-ditrifluoromethylpropiophenone,
2-Bromo-2'-fluoropropiophenone,
2-Bromopropiophenone,
2-Bromo-4'-fluoropropiophenone,
2-Bromo-3'-nitropropiophenone,
2-Bromo-3'-chloropropiophenone,
2-Bromo-4'-methylpropiophenone,
2-Bromo-3'-nitropropiophenone,
2-Bromo-2',5'-dichloropropiophenone,
2-Bromo-3'-nitropropiophenone,
2-Bromo-1-(2-pyridyl)-1-propanone,
2-Bromo-1-(2-naphthyl)-1-propanone,
2-Bromo-4'-methoxypropiophenone,
2-Bromo-1-(3-pyridyl)-1-propanone,
2-Bromo-1-(2-thienyl)-1-propanone,
2-Bromo-3',4'-dichloropropiophenone,
2-Bromo-4'-chloropropiophenone,
2-Bromo-4'-bromopropiophenone,
2-Bromo-4'-benzyloxypropiophenone,
2-Bromo-4'-ethoxypropiophenone,
2-Bromo-4'-hydroxypropiophenone,
2-Bromo-2',5'-dimethoxypropiophenone,
2-Bromo-3'-bromopropiophenone,
2-Bromo-3'-chloropropiophenone,
2-Bromo-2'-methoxypropiophenone,
2-Bromo-3',4'-methylenedioxypropiophenone,
2-Bromo-2',4'-dichloropropiophenone,
2-Bromo-1-(2-furyl)-1-propanone,
2-Bromo-1-(4-pyridyl)-1-propanone,
3-Bromo-4-chromanone,
2-Bromo-2'-chloropropiophenone,
2-Bromo-2'-methoxypropiophenone,
2-Bromo-2',5'-difluoropropiophenone,
2-Bromo-2'-methylpropiophenone,
2-Bromo-2',6'-difluoropropiophenone,
2-Bromo-4'-trifluoromethylpropiophenone,
2-Bromo-3'-trifluoromethylpropiophenone,
2-Bromo-3'-methoxycarbonylpropiophenone,
2-Bromo-5'-fluoro-2'-methoxypropiophenone.

Reference Example 2

2-Cyanoacetamidine

To saturated ammonia/ethanol (20 ml) was added ethyl 2-cyanoacetimidate hydrochloride (3.7 g) under ice-cooling, and the mixture was stirred at the same temperature for 0.5 hour and then at room temperature for 2 hours. The precipitated was filtered off and the filtrate was concentrated under reduced pressure on a water bath to remove the excess ammonia. The, residue was used as it was in the next reaction.

Reference Example 3

3-Amino-3-morpholinoacrylonitrile

In anhydrous ethanol (10 ml) was dissolved ethyl 2-cyanoacetimidate (1.0 g), followed by addition of morpholine (0.78 g). The mixture was stirred at room temperature for 4 hours, and the separated crystals were collected by filtration. This crystal crop was used as it was in the next reaction.

Reference Example 4

Carbamoylacetamidine

The title compound was synthesized by the known process (J. Amer. Chem. Soc., 73, 2760, 1951).

Reference Example 5

1-(2-Fluorophenyl)-1-acetimido-2-propanone

A mixture of 2-fluorophenylglycine (5.0 g), pyridine (15.6 g), and acetic anhydride (25.7 g) was heated at 140-150°C for 4 hours. This reaction mixture was concentrated under reduced pressure and the residue was diluted with diethyl ether. The ether layer was washed with water and a saturated aqueous solution of sodium hydrogen carbonate. The ether layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluent: n-hexane/ethyl acetate) to provide the title compound as yellow oily substance (4.7 g).

The following compounds were synthesized in the similar manner as described in Reference Example 5.

1-Phenyl-1-acetamido-2-propanone,
1-(4-Fluorophenyl)-1-acetamido-2-propanone,
3-Acetamido-2-butanone,
1-(3-Nitrophenyl)-1-acetamido-2-propanone,
4-Phenyl-3-acetamido-2-butanone,
1-Phenyl-1-propanamido-2-butanone,
4-(4-Hydroxyphenyl)-3-acetamido-2-butanone,
1-Phenyl-1-isobutanamido-3-methyl-2-butanone,
2-Propanamido-3-pentanone,
4-(Indol-3-yl)-3-acetamido-2-butanone,
1-(3-Chlorophenyl)-1-acetamido-2-propanone
1-Phenyl-1-butanamido-2-pentanone,
3-Acetamido-2-pentanone,
4-(4-Chlorophenyl)-3-acetamido-2-butanone,
1-(3-Pyridyl)-1-acetamido-2-propanone,
1-(2,5-Dichlorophenyl)-1-acetamido-2-propanone,
1-(2-Pyridyl)-1-acetamido-2-propanone,
1-(2-Naphthyl)-1-acetamido-2-propanone,
1-(4-Methoxyphenyl)-1-acetamido-2-propanone.

Reference Example 6

1,1-Dicyano-2-phenyl-2-(1-bromoethyl)ethylene

Propiophenone (30 g) and malononitrile (15 g) were added to benzene (100 ml), followed by addition of acetic acid (5.45 g) and ammonium acetate (1.8 g), the mixture was refluxed for 8 hours, while the byproduct water was continuously distilled off. After cooling to room temperature, the reaction mixture was washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. The residual black oily substance was subjected to vacuum distillation to provide a pale yellow oily substance (32.5 g) (b.p. 120-125°C/2-3 mmHg).

The obtained compound (3.6 g) was dissolved in anhydrous benzene (30 ml), followed by addition of N-bromosuccinimide (3.6 g) and benzoyl peroxide (a catalyst amount), and the mixture was refluxed for 14 hours. After cooling to room temperature, the reaction mixture was filtered to remove insoluble matter and the filtrate was distilled under reduced pressure to remove the solvent. The residual tan oily substance was recrystallized from ethanol to provide the title compound as light-yellow crystals (2.99 g).

Reference Example 7

Sodium cyanoacetone enolate

A solution of 5-methylisoxazole (16.6 g) in ethanol was added dropwise to a solution of sodium ethoxide in ethanol (prepared from 4.6 g of sodium metal and 150 ml of ethanol) under ice-cooling. After completion of dropwise addition, the mixture was stirred at room temperature for 2 hours. Then, ether (150 ml) was added thereto and the mixture was further stirred for several minutes under ice-cooling. The sodium salt was then collected by filtration, washed with ether, and dried in vacuo to provide the title compound as colorless powder (18.1 g).

Reference Example 8

2-Acetyl-3-(2-fluorobenzoyl)butyronitrile

To a solution of 2-bromo-2'-fluoropropiophenone (3.45 g) in ethanol (40 ml) was added a solution of sodium cyanoacetone enolate (1.57 g), as obtained in Reference Example 7, in ethanol (15 ml) dropwise under ice-cooling and the mixture was stirred for 18 hours. The solvent was then distilled off under reduced pressure and the resulting residue was dissolved in ethyl acetate. This solution was washed with water and dried over $MgSO_4$, and the solvent was distilled off under reduced pressure. The resulting residual oily substance was purified by silica gel column chromatography [Wakogel C-200, 110 g; eluent: ethyl acetate/n-hexane (4:1)] to provide the title compound as yellow oily substance (1.43 g).

The following compounds were synthesized in the similar manner as described in Reference Example 8.

2-Acetyl-3-benzoylbutyronitrile
2-Acetyl-3-(3-isopropoxybenzoyl)propionitrile,
2-Acetyl-3-(4-trifluoromethoxybenzoyl)propionitrile,
2-Acetyl-3-(3-trifluoromethylbenzoyl)propionitrile,
2-Acetyl-3-(3-trifluoromethoxybenzoyl)propionitrile,
2-Acetyl-3-[4-(2-methoxy)ethoxybenzoyl]propionitrile,
2-Acetyl-3-(2-fluorobenzoyl)propionitrile,
2-Acetyl-3-(benzofuran-2-carbonyl)propionitrile,
2-Acetyl-3-(3,4-methylenedioxybenzoyl)propionitrile,
2-Acetyl-3-(2,5-difluorobenzoyl)propionitrile,
2-Acetyl-3-(4-chloro-3-methylbenzoyl)propionitrile,
2-Acetyl-3-(2-naphthoyl)propionitrile,
2-Acetyl-3-(3-bromobenzoyl)propionitrile,
2-Acetyl-3-(3-chloro-4-methylbenzoyl)butyronitrile,
2-Acetyl-3-(4-fluorobenzoyl)propionitrile,
2-Acetyl-3-(4-methanesulfonylaminobenzoyl)propionitrile,
2-Acetyl-3-(2-furoyl)butyronitrile,
2-Acetyl-3-(3-chlorobenzoyl)butyronitrile,
2-Acetyl-3-(3-methoxybenzoyl)propionitrile.

Example 1

2-Amino-3-cyano-4-methyl-5-(2,5-difluorophenyl)pyrrole (compound No. 63)

To an ethanolic solution of 2-cyanoacetamidine obtained from ethyl 2-cyanoacetimidate hydrochloride (3.7 g) as in Reference Example 2, was added a solution of 2-bromo-2',5'-difluoropropiophenone (3.7 g) in ethanol dropwise under ice-cooling with stirring, and the mixture was further stirred at room temperature overnight. This reaction mixture was poured into iced water and the separated crystal crop was collected by filtration. This crude product was dissolved in ethyl acetate. The ethyl acetate layer was washed with water, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Wakogel C-200, 200 g; eluent: chloroform) and recrystallized from benzene-n-hexane to provide the title compound as yellow powder (0.58 g). m.p. 146-147°C.

Elemental analysis ($C_{12}H_9F_2N_3$)			
Calcd. (%):	C, 61.80;	H, 3.89;	N, 18.02
Found (%):	C, 61.71;	H, 3.91;	N, 17.69

Example 2

3-Cyano-5-(4-fluorophenyl)-4-methyl-2-morpholinopyrrole (compound No. 72)

In anhydrous ethanol (10 ml) was dissolved 3-amino-3-morpholinoacrylonitrile, as prepared from ethyl 2-cyanoacetimidate (1.0 g) and morpholine (0.78 g) as in Reference Example 3, followed by addition of sodium hydrogen carbonate (0.95 g). Then, a solution of 2-bromo-4'-fluoropropiophenone (2.06 g) in ethanol was added dropwise thereto at room temperature with stirring. The mixture was refluxed for 10 minutes and, then, stirred at room temperature overnight. The separated crystal crop was collected by filtration and recrystallized from ethanol to provide the title compound as colorless crystals (0.12 g). m.p. 245-247°C.

Elemental analysis ($C_{16}H_{16}FN_3O$)			
Calcd. (%):	C, 67.35;	H, 5.65;	N, 14.73
Found (%):	C, 67.14;	H, 5.86;	N, 14.69

Example 3

2-Amino-3-cyano-4H-[1]benzopyrano[4,3-b]pyrrole (compound No. 52)

To an ethanolic solution of 2-cyanoacetamidine prepared from ethyl 2-cyanoacetimidate hydrochloride (4.0 g) as in Reference Example 2 was added a solution of 3-bromo-4-chromanone (3.0 g) in ethanol dropwise under ice-cooling with stirring. The mixture was stirred at room temperature overnight and, then, concentrated under reduced pressure. The resulting crude product was dissolved in ethyl acetate. The ethyl acetate layer was washed with water, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Wakogel C-200, 200 g; eluent: 2% methanol/chloroform) and recrystallized from acetone/isopropyl ether to provide the title compound as light-brown crystals (0.31 g). m.p. 216-217°C.

Elemental analysis ($C_{12}H_9N_3O$)			
Calcd. (%):	C, 68.24;	H, 4.29;	N, 19.89
Found (%):	C, 68.29;	H, 4.52;	N, 19.81

Example 4

2-Amino-3-carbamoyl-4-methyl-5-phenylpyrrole (compound No. 76)

To a solution (20 ml) of carbamoylacetamidine (5.1 g) in ethanol was added a solution of 2-bromopropiophenone (4.0 g) in ethanol dropwise thereto under ice-cooling with stirring and the mixture was then stirred at room temperature overnight. The insoluble matter was filtered off and the filtrate was concentrated under reduced pressure. The obtained product was washed with benzene, purified by silica gel column chromatography (Wakogel C-200, 200 g; eluent: 50% ethyl acetate/n-hexane), and recrystallized from ethyl acetate/diethyl ether to provide the title compound as colorless crystals (0.2 g), m.p. 195-197°C.

Elemental analysis ($C_{12}H_{13}N_3O$)			
Calcd. (%):	C, 66.96;	H, 6.09;	N, 19.52
Found (%):	C, 66.95;	H, 6.23;	N, 19.38

Example 5-(1)

2-Amino-3-cyano-4-methyl-5-(2-fluorophenyl)pyrrole (compound No. 1)

1-(2-Fluorophenyl)-1-acetamido-2-propanone (3.13 g) and malononitrile (1.49 g) were dissolved in methanol (15 ml) and the solution was stirred under ice-cooling. Then, 55% aqueous solution of potassium hydroxide was added to the above solution to adjust to pH 10. The reaction mixture was then warmed and stirred at 55-60°C for 0.5 hour. After cooling, the reaction mixture was poured into iced water and the resulting crystals were collected by filtration. This crude crystalline product was recrystallized from methanol-water and, further, from benzene to provide the title compound as colorless crystals (0.72 g), m.p. 117-118°C

Elemental analysis ($C_{12}H_{10}FN_3$)			
Calcd. (%):	C, 66.97;	H, 4.68;	N, 19.52
Found (%):	C, 67.09;	H, 4.74;	N, 19.40

Example 5-(2)

2-Amino-3-cyano-4-methyl-5-(2-fluorophenyl)pyrrole (compound No. 1: an alternative process)

To an ethanolic solution of 2-cyanoacetamidine prepared from 10 g of ethyl 2-cyanoacetimidate hydrochloride as in Reference Example 2 was added a solution of 2-bromo-2'-fluoropropiophenone (7.6 g) in ethanol dropwise under ice-cooling with stirring, and the mixture was then stirred at room temperature overnight. This reaction mixture was poured into iced water (500 g) and the resulting crystals were collected by filtration. The crude crystal crop was washed well with n-hexane, air-dried, and purified by flash chromatography (Kieselgel 60H, 90 g; eluent: 30% ethyl acetate/n-hexane). Recrystallization from benzene-n-hexane (1:1) yielded the title compound as colorless crystals (4.67 g). The physical constants of this product were in agreement with those of the product obtained in Example 5-(1).

Example 6

2-Amino-3-cyano-1-methoxycarbonylamino-4-methyl-5-phenylpyrrole (compound No. 13)

In anhydrous ethanol (30 ml) was suspended 1,1-dicyano-2-phenyl-2-(1-bromoethyl)ethylene (1.3 g) and while the suspension was stirred at 65°C, 10 ml of a suspension of methyl hydrazinecarboxylate (1.3 g) in anhydrous ethanol was added dropwise over about 5 minutes. The mixture was stirred at the same temperature for 4.5 hours and poured in iced water (200 g), and the resulting crystals were collected by filtration. The resulting crystals (1.0 g) were purified by

silica gel column chromatography (Wakogel C-200, 200 g; eluent: 30% ethyl acetate/n-hexane) and recrystallized from ethyl acetate/isopropyl ether to provide the title compound as colorless needles (0.48 g). m.p. 178-179°C.

Elemental analysis ($C_{14}H_{14}N_4O_2$)			
Calcd. (%):	C, 62.21;	H, 5.22;	N, 20.73
Found (%):	C, 62.25;	H, 4.92;	N, 20.72

Example 7

3-Cyano-4-methyl-2-methylamino-5-phenylpyrrole (compound No. 75)

2-Amino-3-cyano-4-methyl-5-phenylpyrrole (compound No. R1) (3.0 g), prepared in the process described in the literature (J. Prakt. Chem., 318, 663, 1976), and ethyl orthoformate (12 ml) were refluxed for 4.5 hours. After cooling the reaction mixture to room temperature, the crystals which had separated out were collected by filtration. This crystal crop was washed with benzene and then petroleum ether, air-dried, and purified by silica gel column chromatography (Wakogel C-200, 200 g; eluent: chloroform) to obtain the iminoether as light-green crystals (1.9 g). This iminoether (1.85 g) was dissolved in anhydrous methanol (37 ml) and while the solution was stirred under ice-cooling, sodium borohydride (0.33 g) was added thereto in small portions. The mixture was stirred under cooling with water for 12 hours, after which the insoluble matter was removed by filtration and washed with benzene. The filtrate and washes were combined and concentrated under reduced pressure and the resulting residue was purified by silica gel column chromatography (Wakogel C-200, 200 g; eluent: chloroform) and recrystallized from benzene/n-hexane to provide the title compound as pale yellow crystals (0.37 g). m.p. 138-139°C.

Elemental analysis ($C_{13}H_{13}N_3$)			
Calcd. (%):	C, 73.91;	H, 6.20;	N, 19.89
Found (%):	C, 73.85;	H, 6.52;	N, 19.66

Example 8

2-Benzylamino-3-cyano-4-methyl-5-(2-fluorophenyl)pyrrole (compound No. 74)

To a solution of 2-amino-3-cyano-4-methyl-5-(2-fluorophenyl)pyrrole (Compound No. 1) obtained in Example 5 (0.21 g) in methylene chloride (5 ml) was added a small amount of magnesium sulfate and the mixture was stirred under ice-cooling. Then, a solution of benzaldehyde (0.11 g) in methylene chloride (5 ml) was added dropwise at the same temperature and the mixture was stirred at room temperature for 5 days. The magnesium sulfate was then filtered off and the filtrate was concentrated under reduced pressure. After the residue was dissolved in methanol (15 ml), sodium borohydride (76 mg) was added thereto under ice-cooling. This mixture was stirred at room temperature for 1 hour and the reaction mixture was concentrated under reduced pressure. To the residue was added ethyl acetate, and the ethyl acetate layer was washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Wakogel C-200, 50 g; eluent: chloroform/methanol = 50/1) and the resulting crystals were recrystallized from benzene/n-hexane to provide the title compound as light-yellow powder (0.17 g). m.p. 151-152°C.

Elemental analysis ($C_{15}H_{16}FN_3$)			
Calcd. (%):	C, 74.74;	H, 5.28;	N, 13.76
Found (%):	C, 74.78;	H, 5.38;	N, 13.50

Example 9

3-Cyano-4-methyl-2-(2-oxopyrrolidin-1-yl)-5-phenylpyrrole (compound No. 73)

To a solution of 3-cyano-4-methyl-2-amino-5-phenylpyrrole (4.9 g) in THF (80 ml) was added triethylamine (2.5 g) and while the mixture was stirred at -50°C, 4-chlorobutyryl chloride (3.5 g) was added. This reaction mixture was then stirred at room temperature for 1.5 hours, after which the insoluble matter was filtered off. The filtrate was diluted with ethyl acetate and the organic layer was washed with water and saturated aqueous solution of sodium hydrogen carbonate, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was recrystallized from benzene/n-hexane. The crystals were suspended in ethanol (40 ml), and potassium tert-butoxide (1.32 g) was added thereto. The mixture was stirred at room temperature overnight and the resulting crystals were collected by filtration, washed with water, and air-dried. The crude crystals thus obtained were recrystallized from ethanol to provide the title compound as light-yellow needles (1.5 g). m.p. 140-141°C.

Elemental analysis ($C_{16}H_{15}N_3O$)			
Calcd. (%):	C, 72.43;	H, 5.70;	N, 15.84
Found (%):	C, 72.42;	H, 5.64;	N, 15.79

Example 10

2-Amino-3-cyano-4-methyl-5-(3-pyridyl)pyrrole hydrochloride (compound No. 14)

2-Amino-3-cyano-4-methyl-5-(3-pyridyl)pyrrole (compound No. 8) obtained in the same manner as Example 1 (5.0 g) was dissolved in methanol (220 ml) under heating, followed by addition of 40% HCl-methanol (4 ml) under ice-cooling with stirring. The separated crystals were collected by filtration, washed with methanol (50 ml) twice and diethyl ether (50 ml) 3 times, and air-dried. The crude crystals thus obtained were recrystallized from methanol to provide the title compound as reddish brown crystals (3.4 g). m.p. 279-281°C.

Elemental analysis ($C_{11}H_{10}N_4 \cdot HCl$)			
Calcd. (%):	C, 56.30;	H, 4.72;	N, 23.89
Found (%):	C, 56.08;	H, 4.80;	N, 23.90

Example 11

5-(3-Chlorophenyl)-3-cyano-2-methylpyrrole (compound No. 84) and 2-(3-chlorophenyl)-3-cyano-5-methylpyrrole (compound No. 83)

N-(3-chlorobenzoyl)alanine (3.5 g) and 2-chloroacrylonitrile (13.3 g) were dissolved in acetic anhydride (100 ml) and the solution was stirred at 80°C for 5 hours. This reaction mixture was concentrated under reduced pressure and the residue was subjected to silica gel column chromatography (Wakogel C-200, 600 g; eluent: methylene chloride) to fractionate the objective compounds. The compounds were respectively recrystallized from benzene/n-hexane.

Compound No. 84 was obtained as light-brown powder (291 mg). m.p. 208-209°C.

Elemental analysis ($C_{12}H_9ClN_2$)			
Calcd. (%):	C, 66.52;	H, 4.19;	N, 12.93
Found (%):	C, 66.47;	H, 4.21;	N, 12.87

Compound No. 83 was obtained as colorless scales (426 mg). m.p. 189-190°C.

Elemental analysis ($C_{12}H_9ClN_2$)			
Calcd. (%):	C, 66.52;	H, 4.19;	N, 12.93
Found (%):	C, 66.51;	H, 4.24;	N, 12.86

Example 12

5-(2-Fluorophenyl)-3-cyano-2,4-dimethylpyrrole (compound No. 194)

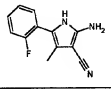
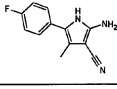
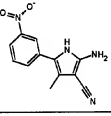
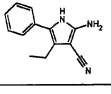
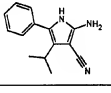
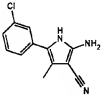
To a solution of 2-acetyl-3-(2-fluorobenzoyl)butyronitrile (1.4g) obtained in Reference Example 8 in acetic acid (15 ml) was added ammonium acetate (6.0 g) and the mixture was stirred at 90°C for 15 minutes. This reaction mixture was poured in iced water and the resulting crystals were collected by filtration. This crystal crop was dissolved in benzene and dried over $MgSO_4$ and the solvent was distilled off under reduced pressure. The residual orange-colored crystals were purified by silica gel column chromatography (Wakogel C-200, 120 g; eluent: chloroform) and the resulting orange-colored powder was recrystallized from benzene/n-hexane to provide the title compound as orange-colored colorless needles (0.36 g) m.p. 125-127°C.

Elemental analysis ($C_{13}H_{11}FN_2$)			
Calcd. (%):	C, 72.88;	H, 5.18;	N, 13.08
Found (%):	C, 73.11;	H, 5.39;	N, 13.08

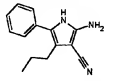
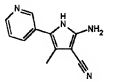
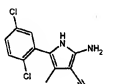
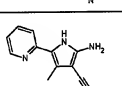
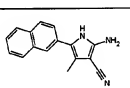
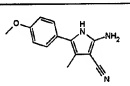
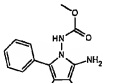
The structural formulas and physicochemical properties of the compounds synthesized in Examples 1-12 and the compounds synthesized in the similar procedures as the Examples (compound Nos. 2-12, 15-51, 53-62, 64-71, 77-82, 85-193, 195-266) are listed in Table 2. However, the present invention is by no means limited to those compounds.

In the column "Synthetic process" of the table, synthetic processes used for the production of the respective compounds are indicated as "A"-"I". "A and B", for instance, in the column means that the same compound was synthesized by both synthetic process A and synthetic process B.

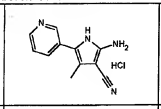
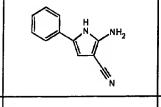
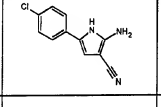
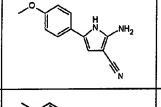
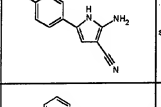
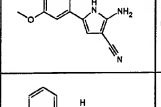
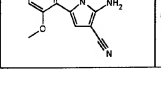
Table 2

Compound No.	Structural formula	m.p. (℃) State	Molecular formula Elemental analysis Calcd. (%) Found (%)	Synthetic process
1		117-118 Colorless crystals	$C_{12}H_{10}FN_3$ C, 66.97; H, 4.68; N, 19.52; C, 67.09; H, 4.74; N, 19.40;	A and B
2		203-204 Greenish brown needles	$C_{12}H_{10}FN_3 \cdot 2/5H_2O$ C, 55.35; H, 4.58; N, 8.60; C, 55.26; H, 4.67; N, 8.45;	A
3		195-196 Brown needles	$C_{12}H_{10}N_4O_2 \cdot 1/10H_2O$ C, 59.06; H, 4.21; N, 22.96; C, 59.05; H, 4.26; N, 22.56;	A
4		131-132 Light-brown powder	$C_{13}H_{13}N_3$ C, 73.91; H, 6.20; N, 19.89; C, 74.10; H, 6.41; N, 19.62;	A
5		104-105 Light-brown powder	$C_{14}H_{15}N_3$ C, 74.64; H, 6.71; N, 18.65; C, 74.75; H, 6.89; N, 18.30;	B
6		205-206 Light-brown powder	$C_{12}H_{10}ClN_3$ C, 62.21; H, 4.35; N, 18.14; C, 62.07; H, 4.50; N, 18.00;	B

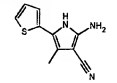
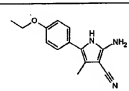
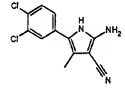
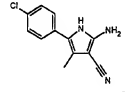
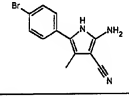
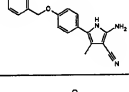
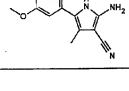
Continuation of Table 2

7		129-130 Light-yellow scales	$C_{14}H_{15}N_3$ C, 74.64; H, 6.71; N, 18.65; C, 74.52; H, 6.66; N, 18.63;	B
8		228-230 Yellow powder	$C_{11}H_{10}N_4$ C, 66.65; H, 5.09; N, 28.26; C, 66.44; H, 5.07; N, 27.95;	A
9		155-156 Colorless prisms	$C_{12}H_9Cl_2N_3 \cdot H_2O$ C, 52.39; H, 3.66; N, 15.27; C, 52.50; H, 3.80; N, 14.84;	A
10		213-214 Yellow scales	$C_{11}H_{10}N_4$ C, 66.65; H, 5.09; N, 28.26; C, 66.46; H, 5.14; N, 28.18;	A
11		203-205 Yellowish green powder	$C_{16}H_{13}N_3$ C, 77.71; H, 5.30; N, 16.99; C, 77.46; H, 5.30; N, 16.74;	A
12		188-189 Light yellow needles	$C_{13}H_{13}N_3O$ C, 68.70; H, 5.77; N, 18.49; C, 68.84; H, 5.73; N, 18.65;	A
13		178-179 Colorless needles	$C_{14}H_{14}N_4O_2$ C, 62.21; H, 5.22; N, 20.73; C, 62.25; H, 4.96; N, 20.72;	D

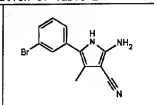
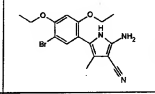
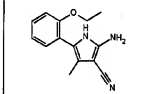
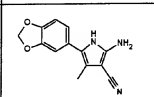
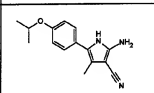
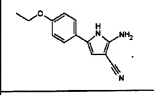
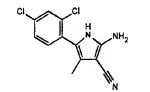
Continuation of Table 2

14		279-281 Reddish brown crystals	$C_{11}H_{10}N_4 \cdot HCl$ C, 56.30; H, 4.72; N, 23.89; C, 56.08; H, 4.80; N, 23.90;	A
15		190-191 Light-purple crystals	$C_{11}H_9N_3$ C, 72.11; H, 4.95; N, 22.94; C, 72.41; H, 5.12; N, 22.87;	A
16		247-248 Gray prisms	$C_{11}H_8ClN_3$ C, 60.70; H, 3.70; N, 19.31; C, 60.73; H, 3.85; N, 19.64;	A
17		216-220 Light-brown crystals	$C_{12}H_{11}N_3O \cdot 1/20H_2O$ C, 67.31; H, 5.22; N, 19.62; C, 67.58; H, 5.14; N, 19.30;	A
18		221-224 silver-colored crystals	$C_{12}H_{11}N_3$ C, 73.07; H, 5.62; N, 21.30; C, 73.00; H, 5.61; N, 21.20;	A
19		159-160 Grayish green crystals	$C_{12}H_{11}N_3O$ C, 67.59; H, 5.20; N, 19.71; C, 67.64; H, 5.23; N, 19.50;	A
20		153-155 Grayish brown crystals	$C_{12}H_{11}N_3O$ C, 67.59; H, 5.20; N, 19.71; C, 67.47; H, 5.30; N, 19.44;	A

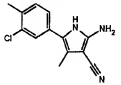
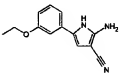
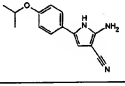
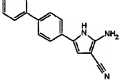
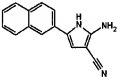
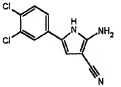
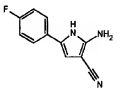
Continuation of Table 2

21		117-118 Light-green crystals	$C_{10}H_8N_3S$ C, 59.09; H, 4.46; N, 20.67; C, 59.26; H, 4.48; N, 20.76;	A
22		166-167 Light-brown crystals	$C_{14}H_{13}N_3O$ C, 69.69; H, 6.27; N, 17.41; C, 69.95; H, 6.25; N, 17.51;	A
23		218-219 Light-brown crystals	$C_{12}H_9Cl_2N_3$ C, 54.16; H, 3.41; N, 15.79; C, 53.82; H, 3.41; N, 15.78;	A
24		212-213 Pale purple crystals	$C_{12}H_{10}ClN_3$ C, 62.21; H, 4.35; N, 18.14; C, 62.39; H, 4.43; N, 18.24;	A
25		206-209 Light-purple cystals	$C_{12}H_{10}BrN_3$ C, 52.19; H, 3.65; N, 15.22; C, 52.07; H, 3.68; N, 15.17;	A
26		160-161 Colorless crystals	$C_{19}H_{17}N_3O$ C, 75.23; H, 5.65; N, 13.85; C, 75.06; H, 5.75; N, 13.80;	A
27		113-115 Gray crystals	$C_{14}H_{13}N_3O_2$ C, 65.36; H, 5.88; N, 16.33; C, 65.17; H, 5.92; N, 16.38;	A

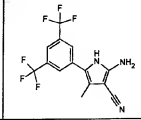
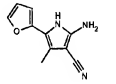
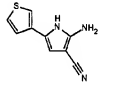
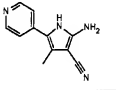
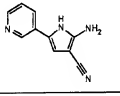
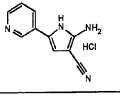
Continuation of Table 2

28		216-218 Pale pink crystals	$C_{12}H_{10}BrN_3$ C, 52.19; H, 3.65; N, 15.22; C, 52.23; H, 3.75; N, 15.28;	A
29		180-181 Green crystals	$C_{16}H_{18}BrN_3O_2$ C, 52.76; H, 4.98; N, 11.54; C, 52.62; H, 5.01; N, 11.32;	A
30		114-117 Light-yellow crystals	$C_{14}H_{13}N_3O$ C, 69.69; H, 6.27; N, 17.41; C, 69.86; H, 6.27; N, 17.37;	A
31		198-200 Gray crystals	$C_{13}H_{11}N_3O_2$ C, 64.72; H, 4.60; N, 17.42; C, 64.76; H, 4.76; N, 17.44;	A
32		118-119 Colorless crystals	$C_{15}H_{17}N_3O$ C, 70.56; H, 6.71; N, 16.46; C, 70.82; H, 6.77; N, 16.60;	A
33		234-237 Light-green cystals	$C_{13}H_{13}N_3O$ C, 68.70; H, 5.77; N, 18.49; C, 68.67; H, 5.94; N, 18.50;	A
34		157-158 Light-pink crystals	$C_{12}H_9Cl_2N_3$ C, 54.16; H, 3.41; N, 15.79; C, 54.34; H, 3.41; N, 15.98;	A

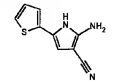
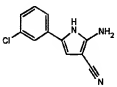
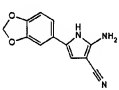
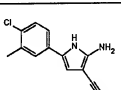
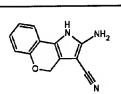
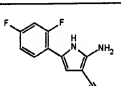
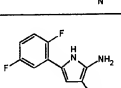
Continuation of Table 2

35		138-140 Light-gray crystals	$C_{13}H_{12}ClN_3$ C, 63.55; H, 4.92; N, 17.10; C, 63.58; H, 4.77; N, 17.06;	A
36		158-159 Light-brown crystals	$C_{13}H_{13}N_3O$ C, 68.70; H, 5.77; N, 18.49; C, 68.87; H, 5.89; N, 18.50;	A
37		177-180 Gray crystals	$C_{14}H_{15}N_3O$ C, 69.69; H, 6.27; N, 17.41; C, 69.53; H, 6.39; N, 17.32;	A
38		278-281 Pale brown crystals	$C_{17}H_{13}N_3$ C, 78.74; H, 5.05; N, 16.20; C, 78.83; H, 5.25; N, 16.30;	A
39		224-226 Light-brown crystals	$C_{15}H_{11}N_3$ C, 77.23; H, 4.75; N, 18.01; C, 77.30; H, 4.96; N, 18.01;	A
40		257-260 Light-brown crystals	$C_{11}H_7Cl_2N_3$ C, 52.41; H, 2.80; N, 16.67; C, 52.46; H, 2.98; N, 16.45;	A
41		214-218 Light-purple crystals	$C_{11}H_8FN_3$ C, 65.67; H, 4.01; N, 20.88; C, 66.03; H, 4.24; N, 20.95;	A

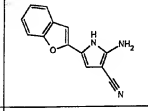
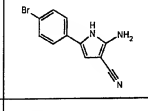
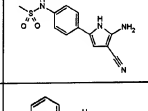
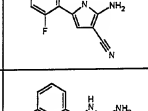
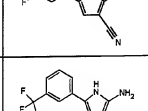
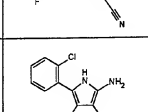
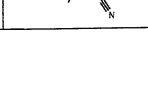
Continuation of Table 2

42		230-231 Light-orange crystals	$C_{14}H_9F_6N_3$ C, 50.46; H, 2.72; N, 12.61; C, 50.71; H, 2.62; N, 12.56;	A
43		155-156 Light-red crystals	$C_{10}H_8N_3O$ C, 64.16; H, 4.85; N, 22.45; C, 64.34; H, 5.11; N, 22.37;	A
44		203-206 Light-purple crystals	$C_9H_7N_3S$ C, 57.12; H, 3.73; N, 22.21; C, 57.32; H, 3.84; N, 22.19;	A
45		215-220 Yellowish brown crystals	$C_{11}H_{10}N_4 \cdot 1/2H_2O$ C, 63.75; H, 5.35; N, 27.04; C, 63.75; H, 5.31; N, 26.74;	A
46		241-244 Light-brown crystals	$C_{10}H_8N_4$ C, 65.21; H, 4.38; N, 30.42; C, 65.38; H, 4.60; N, 30.56;	A
47		≧275 Orange-colored crystals	$C_{10}H_8N_4 \cdot HCl$ C, 54.43; H, 4.11; N, 25.39; C, 54.31; H, 4.31; N, 25.41;	A

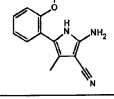
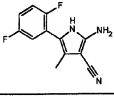
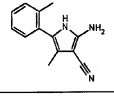
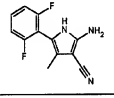
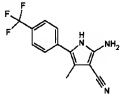
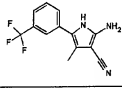
Continuation of Table 2

48		180-181 Gray crystals	$C_8H_7N_3S$ C, 57.12; H, 3.73; N, 22.21; C, 57.20; H, 3.78; N, 22.08;	A
49		192-193 Brown crystals	$C_{11}H_8ClN_3$ C, 60.70; H, 3.70; N, 19.31; C, 60.88; H, 3.67; N, 19.34;	A
50		235-239 Light-gray crystals	$C_{12}H_9N_3O_2$ C, 63.43; H, 3.99; N, 18.49; C, 63.52; H, 4.00; N, 18.47;	A
51		234-237 Purple crystals	$C_{12}H_{10}ClN_3$ C, 62.21; H, 4.35; N, 18.14; C, 62.18; H, 4.24; N, 18.17;	A
52		216-217 Light-brown prisms	$C_{12}H_9N_3O$ C, 68.24; H, 4.29; N, 19.89; C, 68.29; H, 4.52; N, 19.81;	A
53		215-217 Light-gray crystals	$C_{11}H_7F_2N_3$ C, 60.28; H, 3.22 ;N, 19.17; C, 60.71; H, 3.53 ;N, 19.31;	A
54		222-224 Gray crystals	$C_{11}H_7F_2N_3$ C, 60.28; H, 3.22; N, 19.17; C, 60.45; H, 3.15; N, 19.22;	A

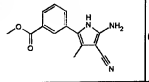
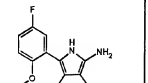
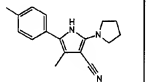
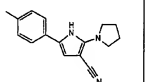
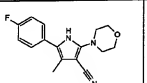
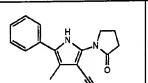
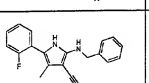
Continuation of Table 2

55		247-251 Pale brown crystals	$C_{13}H_9N_3O$ C, 69.95; H, 4.06; N, 18.82; C, 70.30; H, 4.04; N, 19.02;	A
56		260-263 Purple crystals	$C_{11}H_8BrN_3$ C, 50.41; H, 3.08; N, 16.03; C, 50.26; H, 3.04; N, 16.07;	A
57		265-270 Light-brown crystals	$C_{12}H_{12}N_4O_2S \cdot 1/5H_2O$ C, 51.49; H, 4.47; N, 20.02; C, 51.67; H, 4.44; N, 19.67;	A
58		189-191 Light-yellow plates	$C_{11}H_8FN_3$ C, 65.67; H, 4.01; N, 20.88; C, 66.15; H, 4.14; N, 20.81;	A
59		192-193 Gray crystals	$C_{11}H_8FN_3 \cdot 1/25C_6H_6$ C, 66.07; H, 4.06; N, 20.57; C, 66.38; H, 4.23; N, 21.01;	A
60		183-184 Light-brown needles	$C_{12}H_8F_3N_3$ C, 57.37; H, 3.21; N, 16.73; C, 57.40; H, 3.14; N, 16.86;	A
61		160-161 Colorless prisms	$C_{12}H_{10}ClN_3$ C, 62.21; H, 4.35; N, 18.14; C, 62.29; H, 4.38; N, 18.55;	A

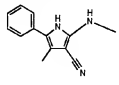
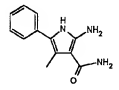
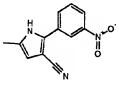
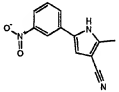
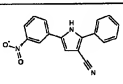
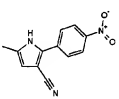
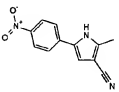
Continuation of Table 2

62		108-109 Colorless needles	$C_{13}H_{13}N_3O \cdot 1/5H_2O$ C, 67.63; H, 5.85; N, 18.20; C, 67.79; H, 5.79; N, 18.22;	A
63		146-147 Yellow powder	$C_{12}H_9F_2N_3$ C, 61.80; H, 3.89; N, 18.02; C, 61.71; H, 3.91; N, 17.69;	A
64		127-128 Pale pink needles	$C_{13}H_{13}N_3$ C, 73.91; H, 6.20; N, 19.89; C, 73.84; H, 6.28; N, 19.76;	A
65		181-182 Yellow powder	$C_{12}H_9F_2N_3$ C, 61.80; H, 3.89; N, 18.02; C, 61.93; H, 3.98; N, 18.09;	A
66		177-178 Light-brown needles	$C_{13}H_{10}F_3N_3$ C, 58.87; H, 3.80; N, 15.84; C, 58.88; H, 3.88; N, 15.96;	A
67		202-203 Colorless needles	$C_{13}H_{10}F_3N_3$ C, 58.87; H, 3.80; N, 15.84; C, 58.58; H, 3.82; N, 15.73;	A

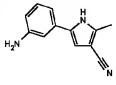
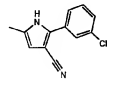
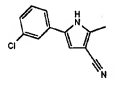
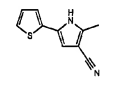
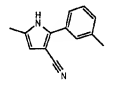
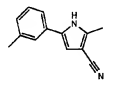
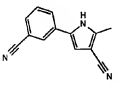
Continuation of Table 2

68		223-225 Greenish brown needles	$C_{14}H_{13}N_3O_2$ C, 65.87; H, 5.13; N, 16.46; C, 65.76; H, 5.19; N, 16.30;	A
69		143-144 Colorless crystals	$C_{13}H_{12}FN_3O$ C, 63.67; H, 4.93; N, 17.13; C, 63.66; H, 4.92; N, 16.84;	A
70		270-272 Yellow crystals	$C_{17}H_{19}N_3$ C, 76.95; H, 7.22; N, 15.84; C, 76.87; H, 7.22; N, 15.95;	A
71		253-260 Light-blue crystals	$C_{16}H_{17}N_3$ C, 76.46; H, 6.82; N, 16.72; C, 76.41; H, 6.61; N, 16.71;	A
72		245-247 Colorless crystals	$C_{16}H_{16}FN_3O$ C, 67.35; H, 5.65; N, 14.73; C, 67.14; H, 5.86; N, 14.69;	A
73		140-141 Light-yellow needles	$C_{16}H_{15}N_3O$ C, 72.43; H, 5.70; N, 15.84; C, 72.42; H, 5.64; N, 15.79;	G
74		151-152 Light-yellow powder	$C_{19}H_{16}FN_3$ C, 74.74; H, 5.28; N, 13.76; C, 74.78; H, 5.38; N, 13.50;	F

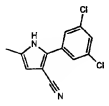
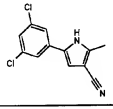
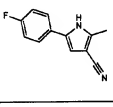
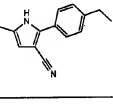
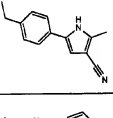
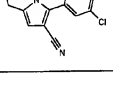
Continuation of Table 2

75		138-139 Light-yellow needles	$C_{13}H_{13}N_3$ C, 73.91; H, 6.20; N, 19.89; C, 73.85; H, 6.72; N, 19.66;	F
76		195-197 Colorless crystals	$C_{12}H_{13}N_3O$ C, 66.96; H, 6.09; N, 19.52; C, 66.95; H, 6.23; N, 19.38;	A
77		247-248 Light-brown needles	$C_{12}H_8N_3O_2$ C, 63.43; H, 3.99; N, 18.49; C, 63.44; H, 3.89; N, 18.53;	H
78		235-236 Orange-colored needles	$C_{12}H_8N_3O_2$ C, 63.43; H, 3.99; N, 18.49; C, 63.35; H, 3.96; N, 18.56;	H
79		239-240 Yellow powder	$C_{17}H_{11}N_3O_2$ C, 70.58; H, 3.83; N, 14.53; C, 70.70; H, 3.93; N, 14.50;	H
80		220-221 Light-yellow needles	$C_{12}H_8N_3O_2$ C, 63.43; H, 3.99; N, 18.49; C, 63.46; H, 4.19; N, 18.17;	H
81		260-262 Light-yellow powder	$C_{12}H_8N_3O_2$ C, 63.43; H, 3.99; N, 18.49; C, 63.27; H, 3.98; N, 18.26;	H

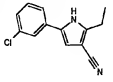
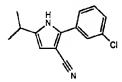
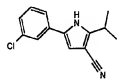
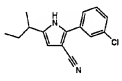
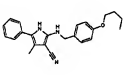
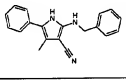
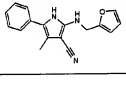
Continuation of Table 2

82		163-164 Colorless prisms	$C_{12}H_{11}N_3$ C, 73.07; H, 5.62; N, 21.30; C, 73.47; H, 5.61; N, 21.38;	I
83		189-190 Colorless scales	$C_{12}H_9ClN_2$ C, 66.52; H, 4.19; N, 12.93; C, 66.51; H, 4.24; N, 12.86;	H
84		208-209 Light-brown powder	$C_{12}H_9ClN_2$ C, 66.52; H, 4.19; N, 12.93; C, 66.47; H, 4.21; N, 12.87;	H
85		160-161 Colorless powder	$C_{10}H_8N_2S \cdot 1/5H_2O$ C, 62.60; H, 4.31; N, 14.60; C, 62.63; H, 4.31; N, 14.64;	H
86		185-186 Colorless powder	$C_{13}H_{12}N_2$ C, 79.56; H, 6.16; N, 14.27; C, 79.45; H, 5.94; N, 14.34;	H
87		170-173 Colorless powder	$C_{13}H_{12}N_2$ C, 79.56; H, 6.16; N, 14.27; C, 79.31; H, 6.19; N, 14.33;	H
88		252-253 Colorless powder	$C_{13}H_9N_3$ C, 75.35; H, 4.38; N, 20.28; C, 75.27; H, 4.39; N, 20.13;	H

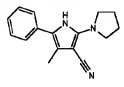
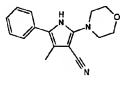
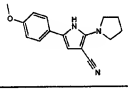
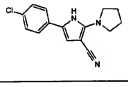
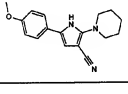
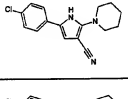
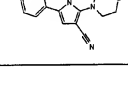
Continuation of Table 2

89		270-271 Colorless powder	$C_{12}H_8Cl_2N_2$ C, 57.40; H, 3.21; N, 11.16; C, 57.15; H, 3.34; N, 11.05;	H
90		275-276 Colorless needles	$C_{12}H_8Cl_2N_2$ C, 57.40; H, 3.21; N, 11.16; C, 57.36; H, 3.34; N, 11.24;	H
91		213-214 Colorless powder	$C_{12}H_8FN_2 \cdot 1/4H_2O$ C, 70.40; H, 4.67; N, 13.68; C, 70.60; H, 4.81; N, 13.88;	H
92		117-118 Colorless powder	$C_{14}H_{14}N_2$ C, 79.97; H, 6.71; N, 13.32; C, 80.13; H, 7.00; N, 13.32;	H
93		176-177 Colorless powder	$C_{14}H_{14}N_2$ C, 79.97; H, 6.71; N, 13.32; C, 80.14; H, 6.65; N, 13.32;	H
94		167-168 Colorless powder	$C_{13}H_{11}ClN_2$ C, 67.68; H, 4.81; N, 12.14; C, 67.56; H, 4.81; N, 12.12;	H

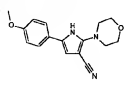
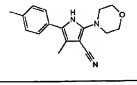
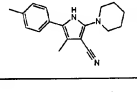
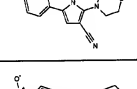
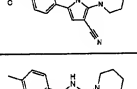
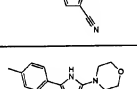
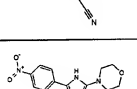
Continuation of Table 2

95		138-139 Colorless powder.	$C_{13}H_{11}ClN_2 \cdot 1/5H_2O$ C, 66.64; H, 4.90; N, 11.96; C, 66.56; H, 4.72; N, 11.87;	H
96		172-173 Colorless powder	$C_{14}H_{13}ClN_2$ C, 68.71; H, 5.35; N, 11.45; C, 68.68; H, 5.62; N, 11.70;	H
97		105-106 Colorless powder	$C_{14}H_{13}ClN_2$ C, 68.71; H, 5.35; N, 11.45; C, 68.71; H, 5.54; N, 11.61;	H
98		91-92 Colorless powder	$C_{15}H_{15}ClN_2 \cdot 1/10H_2O$ C, 69.15; H, 5.88; N, 10.75; C, 68.96; H, 6.09; N, 10.68;	H
99		167-168 Light-yellow powder	$C_{23}H_{25}N_3O$ C, 76.85; H, 7.01; N, 11.69; C, 76.60; H, 7.18; N, 11.68;	F
100		180-182 Light-yellow scales	$C_{19}H_{17}N_3$ C, 79.41; H, 5.96; N, 14.62; C, 80.00; H, 6.05; N, 14.43;	F
101		144-146 Colorless needles	$C_{17}H_{15}N_3O$ C, 73.63; H, 5.45; N, 15.15; C, 73.37; H, 5.39; N, 14.91;	F

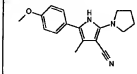
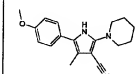
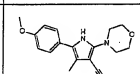
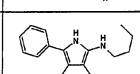
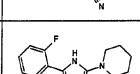
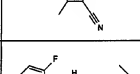
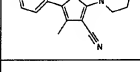
Continuation of Table 2

102		235-237 Colorless crystals	$C_{16}H_{17}N_3$ C, 76.46; H, 6.82; N, 16.72; C, 76.37; H, 6.82; N, 16.54;	A
103		218-219 Colorless crystals	$C_{16}H_{17}N_3O$ C, 71.89; H, 6.41; N, 15.72; C, 71.68; H, 6.12; N, 15.73;	A
104		233-236 Light-yellow crystals	$C_{16}H_{17}N_3O$ C, 71.89; H, 6.41; N, 15.72; C, 71.88; H, 6.40; N, 15.59;	A
105		264-265 Light-blue crystals	$C_{15}H_{14}ClN_3 \cdot 1/10H_2O$ C, 65.86; H, 5.23; N, 15.36; C, 65.62; H, 4.89; N, 15.28;	A
106		191-192 Light-brown crystals	$C_{17}H_{19}N_3O$ C, 72.57; H, 6.81; N, 14.94; C, 72.71; H, 6.96; N, 15.09;	A
107		256-258 Colorless crystals	$C_{16}H_{16}ClN_3$ C, 67.25; H, 5.64; N, 14.70; C, 67.14; H, 5.64; N, 14.78;	A
108		260-262 Blue crystals	$C_{15}H_{14}ClN_3O$ C, 62.61; H, 4.90; N, 14.60; C, 62.33; H, 5.05; N, 14.71;	A

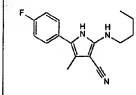
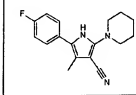
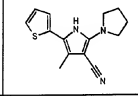
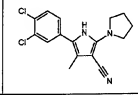
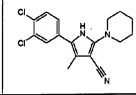
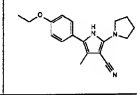
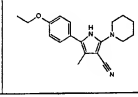
Continuation of Table 2

109		226-228 Light-blue crystals	$C_{16}H_{17}N_3O_2$ C, 67.83; H, 6.05; N, 14.83; C, 67.79; H, 6.15; N, 14.66;	A
110		227-228 Light-yellow crystals	$C_{17}H_{19}N_3O$ C, 72.57; H, 6.81; N, 14.94; C, 72.39; H, 6.87; N, 14.86;	A
111		225-228 Light-yellow crystals	$C_{18}H_{21}N_3$ C, 77.38; H, 7.58; N, 15.04; C, 77.08; H, 7.50; N, 15.03;	A
112		271-273 Blue needles	$C_{15}H_{14}BrN_3O$ C, 54.23; H, 4.25; N, 12.65; C, 54.22; H, 4.45; N, 12.62;	A
113		281-283 Reddish brown needles	$C_{15}H_{16}N_4O_2$ C, 64.85; H, 5.44; N, 18.91; C, 64.74; H, 5.52; N, 18.82;	A
114		239-240 Blue plates	$C_{17}H_{19}N_3$ C, 76.95; H, 7.22; N, 15.84; C, 76.91; H, 7.05; N, 15.82;	A
115		219-220 Light-blue crystals	$C_{16}H_{17}N_3O$ C, 71.89; H, 6.41; N, 15.72; C, 71.81; H, 6.73; N, 15.70;	A
116		≧300 Reddish brown needles	$C_{15}H_{14}N_4O_3$ C, 60.40; H, 4.73; N, 18.78; C, 60.30; H, 5.01; N, 18.63;	A

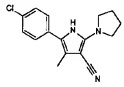
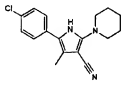
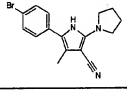
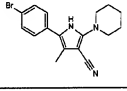
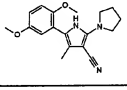
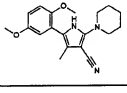
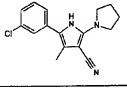
Continuation of Table 2

117		233-236 Light-pink needles	$C_{17}H_{19}N_3O$ C, 72.57; H, 6.81; N, 14.94; C, 72.55; H, 6.45; N, 14.88;	A
118		194-195 Light-brown crystals	$C_{18}H_{21}N_3O$ C, 73.19; H, 7.17; N, 14.23; C, 73.20; H, 7.49; N, 14.22;	A
119		200-202 Light-brown crystals	$C_{17}H_{19}N_3O_2$ C, 68.67; H, 6.44; N, 14.13; C, 68.49; H, 6.55; N, 14.05;	A
120		163-164 Light-brown crystals	$C_{16}H_{19}N_3$ C, 75.85; H, 7.56; N, 16.59; C, 75.60; H, 7.86; N, 16.48;	A
121		181-182 Colorless crystals	$C_{17}H_{16}FN_3$ C, 72.06; H, 6.40; N, 14.83; C, 72.03; H, 6.62; N, 14.85;	A
122		112-114 Colorless powder	$C_{16}H_{18}FN_3$ C, 70.83; H, 6.69; N, 15.49; C, 71.30; H, 6.46; N, 15.51;	A
123		245-250 Colorless crystals	$C_{16}H_{16}FN_3$ C, 71.35; H, 5.99; N, 15.60; C, 71.32; H, 6.01; N, 15.64;	A

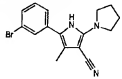
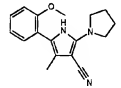
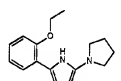
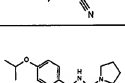
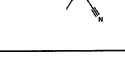
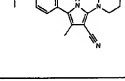
Continuation of Table 2

124		145-146 Colorless crystals	$C_{16}H_{18}FN_3$ C, 70.83; H, 6.69; N, 15.49; C, 70.81; H, 6.50; N, 15.62;	A
125		228-229 Colorless crystals	$C_{17}H_{18}FN_3$ C, 72.06; H, 6.40; N, 14.83; C, 72.27; H, 6.48; N, 14.43;	A
126		215-217 Light-brown crystals	$C_{14}H_{15}N_3S$ C, 65.34; H, 5.88; N, 16.33; C, 65.48; H, 6.14; N, 16.26;	A
127		260-265 Colorless crystals	$C_{16}H_{15}Cl_2N_3$ C, 60.01; H, 4.72; N, 13.12; C, 60.17; H, 4.93; N, 13.09;	A
128		207-209 Colorless crystals	$C_{17}H_{17}Cl_2N_3$ C, 61.09; H, 5.13; N, 12.57; C, 61.06; H, 5.31; N, 12.53;	A
129		220-226 Colorless crystals	$C_{18}H_{21}N_3O$ C, 73.19; H, 7.17; N, 14.23; C, 73.00; H, 7.29; N, 14.41;	A
130		207-212 Colorless crystals	$C_{19}H_{23}N_3O$ C, 73.76; H, 7.49; N, 13.58; C, 73.70; H, 7.58; N, 13.52;	A

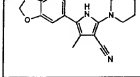
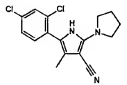
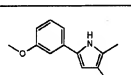
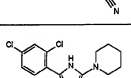
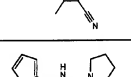
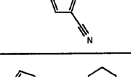
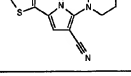
Continuation of Table 2

131		270-272 Colorless crystals	$C_{16}H_{16}ClN_3$ C, 67.25; H, 5.64; N, 14.70; C, 67.27; H, 5.70; N, 14.61;	A
132		250-252 Colorless crystals	$C_{17}H_{18}ClN_3$ C, 68.11; H, 6.05; N, 14.02; C, 68.13; H, 6.22; N, 13.78;	A
133		243-245 Colorless crystals	$C_{16}H_{16}BrN_3$ C, 58.19; H, 4.88; N, 12.72; C, 58.05; H, 4.94; N, 12.89;	A
134		249-253 Colorless crystals	$C_{17}H_{18}BrN_3$ C, 59.31; H, 5.27; N, 12.21; C, 59.21; H, 5.37; N, 12.28;	A
135		168-170 Colorless crystals	$C_{18}H_{21}N_3O_2$ C, 69.43; H, 6.80; N, 13.49; C, 69.42; H, 6.89; N, 13.63;	A
136		176-178 Colorless crystals	$C_{19}H_{23}N_3O_2$ C, 70.13; H, 7.12; N, 12.91; C, 70.07; H, 7.32; N, 12.93;	A
137		231-233 Light-yellow crystals	$C_{16}H_{16}ClN_3$ C, 67.25; H, 5.64; N, 14.70; C, 67.41; H, 5.54; N, 14.83;	A

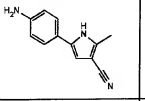
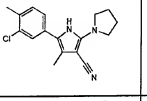
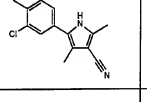
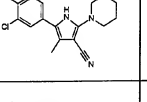
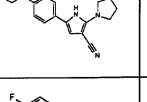
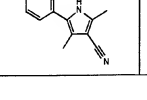
Continuation of Table 2

138		246-248 Light-brown crystals	$C_{16}H_{16}BrN_3$ C, 58.19; H, 4.88; N, 12.72; C, 58.08; H, 4.96; N, 12.76;	A
139		219-220 Light-gray crystals	$C_{17}H_{19}N_3O$ C, 72.57; H, 6.81; N, 14.94; C, 72.50; H, 6.86; N, 14.84;	A
140		171-172 Colorless crystals	$C_{16}H_{21}N_3O$ C, 73.19; H, 7.17; N, 14.23; C, 73.15; H, 7.00; N, 14.23;	A
141		229-235 Light-brown crystals	$C_{19}H_{23}N_3O$ C, 73.76; H, 7.49; N, 13.58; C, 73.55; H, 7.54; N, 13.45;	A
142		242-246 Colorless crystals	$C_{20}H_{25}N_3O$ C, 74.27; H, 7.79; N, 12.99; C, 74.09; H, 7.52; N, 12.96;	A
143		245-252 Light-brown crystals	$C_{17}H_{17}N_3O_2$ C, 69.14; H, 5.80; N, 14.23; C, 69.24; H, 5.83; N, 14.36;	A

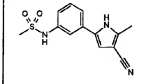
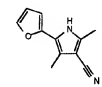
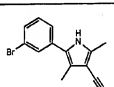
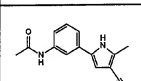
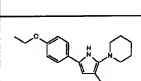
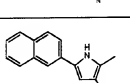
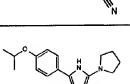
Continuation of Table 2

144		192-195 Light-blue crystals	$C_{16}H_{19}N_3O_2$ C, 69.88; H, 6.19; N, 13.58; C, 69.81; H, 6.17; N, 13.71;	A
145		246-247 Light-brown crystals	$C_{16}H_{15}Cl_2N_3$ C, 60.01; H, 4.72; N, 13.12; C, 60.03; H, 4.70; N, 13.13;	A
146		167-168 Light-gray needles	$C_{13}H_{12}N_2O$ C, 73.56; H, 5.70; N, 13.20; C, 73.69; H, 5.65; N, 13.14;	I
147		215-217 Light-brown crystals	$C_{17}H_{17}Cl_2N_3$ C, 61.09; H, 5.13; N, 12.57; C, 61.01; H, 5.19; N, 12.54;	A
148		224-229 Light-brown crystals	$C_{13}H_{13}N_3S$ C, 64.17; H, 5.39; N, 17.27; C, 64.16; H, 5.29; N, 17.31;	A
149		205-207 Light-green crystals	$C_{14}H_{15}N_3S$ C, 65.34; H, 5.88; N, 16.33; C, 65.23; H, 5.93; N, 16.11;	A
150		190-192 Light-brown powder	$C_{13}H_{11}ClN_2$ C, 67.68; H, 4.81; N, 12.14; C, 67.78; H, 4.93; N, 12.21;	I

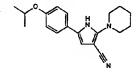
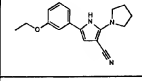
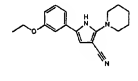
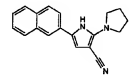
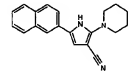
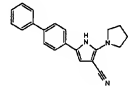
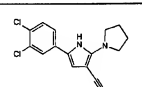
Continuation of Table 2

151		184-185 Ocherous needles	$C_{12}H_{11}N_3$ C, 73.07; H, 5.62; N, 21.30; C, 73.39; H, 5.52; N, 21.24;	I
152		243-249 Light-brown crystals	$C_{17}H_{18}ClN_3$ C, 68.11; H, 6.05; N, 14.02; C, 68.25; H, 6.14; N, 13.96;	A
153		187-188 Colorless needles	$C_{14}H_{13}ClN_2$ C, 68.71; H, 5.35; N, 11.45; C, 68.77; H, 5.46; N, 11.40;	I
154		206-207 Colorless crystals	$C_{18}H_{20}ClN_3$ C, 68.89; H, 6.42; N, 13.39; C, 68.78; H, 6.55; N, 13.41;	A
155		210-213 Light-brown crystals	$C_{17}H_{19}N_3O$ C, 72.57; H, 6.81; N, 14.94; C, 72.39; H, 6.92; N, 14.83;	A
156		199-201 Light-red needles	$C_{13}H_{11}FN_2$ C, 72.88; H, 5.18; N, 13.08; C, 73.15; H, 5.04; N, 13.13;	I

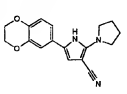
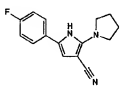
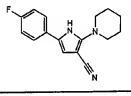
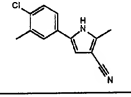
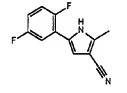
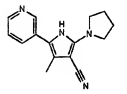
Continuation of Table 2

157		221-222 Light-yellow crystals	$C_{13}H_{13}N_3O_2S \cdot 1/10H_2O$ C, 56.34; H, 4.80; N, 15.16; C, 56.23; H, 4.62; N, 15.02;	I
158		140-142 Light-yellow needles	$C_{11}H_{10}N_2O$ C, 70.95; H, 5.41; N, 15.04; C, 71.07; H, 5.70; N, 15.11;	I
159		195-196 Colorless needles	$C_{13}H_{11}BrN_2$ C, 56.75; H, 4.03; N, 10.18; C, 56.54; H, 4.06; N, 10.14;	I
160		221-222 Light-yellow needles	$C_{14}H_{13}N_3O \cdot 1/5H_2O$ C, 69.23; H, 5.56; N, 17.30; C, 69.26; H, 5.58; N, 17.19;	I
161		211-213 Light-brown crystals	$C_{16}H_{21}N_3O$ C, 73.19; H, 7.17; N, 14.23; C, 73.07; H, 7.37; N, 14.16;	A
162		203-204 Gray powder	$C_{16}H_{12}N_2$ C, 82.73; H, 5.21; N, 12.06; C, 82.91; H, 5.40; N, 12.03;	I
163		200-202 Light-brown crystals	$C_{16}H_{21}N_3O$ C, 73.19; H, 7.17; N, 14.23; C, 73.07; H, 7.33; N, 13.99;	A

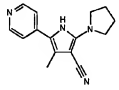
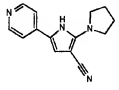
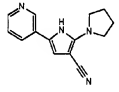
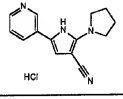
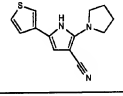
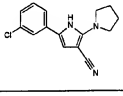
Continuation of Table 2

164		219-223 Light-brown crystals	$C_{19}H_{23}N_3O \cdot 1/10H_2O$ C, 73.33; H, 7.77; N, 13.50; C, 73.17; H, 7.57; N, 13.28;	A
165		297-301 Light-yellow powder	$C_{17}H_{19}N_3O$ C, 72.57; H, 6.81; N, 14.94; C, 72.17; H, 6.45; N, 14.92;	A
166		140-141 Light-blue crystals	$C_{16}H_{21}N_3O \cdot 1/10H_2O$ C, 72.75; H, 7.19; N, 14.14; C, 72.60; H, 7.18; N, 14.06;	A
167		258-261 Light-yellow crystals	$C_{19}H_{17}N_3 \cdot 1/10H_2O$ C, 78.92; H, 6.00; N, 14.53; C, 78.81; H, 6.23; N, 14.67;	A
168		240-243 Brown crystals	$C_{20}H_{19}N_3 \cdot 1/10H_2O$ C, 79.23; H, 6.38; N, 13.86; C, 79.08; H, 6.59; N, 13.71;	A
169		227-231 Brown crystals	$C_{21}H_{19}N_3$ C, 80.48; H, 6.11; N, 13.41; C, 80.23; H, 6.17; N, 13.45;	A
170		257-260 Light-yellow crystals	$C_{15}H_{13}Cl_2N_3$ C, 58.84; H, 4.28; N, 13.72; C, 58.51; H, 4.25; N, 13.83;	A

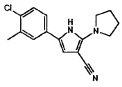
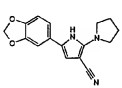
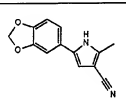
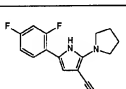
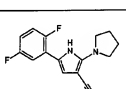
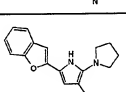
Continuation of Table 2

171		216-221 Light-brown crystals	$C_{17}H_{17}N_3O_2$ C, 69.14; H, 5.80; N, 14.23; C, 69.27; H, 5.68; N, 14.27;	A
172		231-236 Light-brown crystals	$C_{15}H_{14}FN_3$ C, 70.57; H, 5.53; N, 16.46; C, 70.56; H, 5.72; N, 16.63;	A
173		203-204 Colorless crystals	$C_{16}H_{16}FN_3$ C, 71.36; H, 5.99; N, 15.60; C, 71.43; H, 6.17; N, 15.64;	A
174		238-240 Gray powder	$C_{13}H_{11}ClN_2$ C, 67.68; H, 4.81; N, 12.14; C, 68.03; H, 4.84; N, 12.22;	I
175		213-215 Gray powder	$C_{12}H_8F_2N_2$ C, 66.05; H, 3.70; N, 12.84; C, 66.13; H, 3.65; N, 12.92;	I
176		235-236 Light-gray crystals	$C_{15}H_{16}N_4$ C, 71.40; H, 6.39; N, 22.21; C, 71.35; H, 6.43; N, 22.03;	A

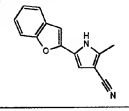
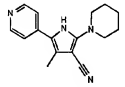
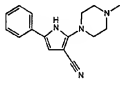
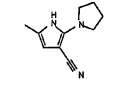
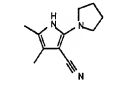
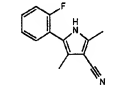
Continuation of Table 2

177		240-242 Brown powder	$C_{15}H_{16}N_4$ C, 71.40; H, 6.39; N, 22.21; C, 71.43; H, 6.49; N, 22.71;	A
178		251-260 Light-brown powder	$C_{14}H_{14}N_4$ C, 70.57; H, 5.92; N, 23.51; C, 70.19; H, 5.99; N, 23.11;	A
179		248-251 Light-purple crystals	$C_{14}H_{14}N_4$ C, 70.57; H, 5.92; N, 23.51; C, 70.58; H, 5.96; N, 23.52;	A
180		270-276 Orange-colored needles	$C_{14}H_{14}N_4 \cdot HCl$ C, 61.20; H, 5.50; N, 20.39; C, 61.23; H, 5.60; N, 20.02;	A
181		230-234 Brown crystals	$C_{13}H_{13}N_3S \cdot 1/7H_2O$ C, 63.50; H, 5.45; N, 17.08; C, 63.91; H, 5.51; N, 16.68;	A
182		220-223 Brown crystals	$C_{15}H_{14}ClN_3 \cdot 1/5H_2O$ C, 65.43; H, 5.27; N, 15.26; C, 65.81; H, 5.15; N, 14.94;	A

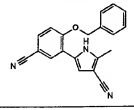
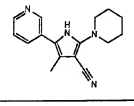
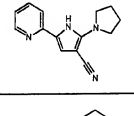
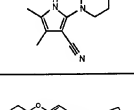
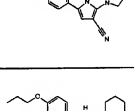
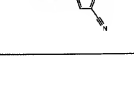
Continuation of Table 2

183		236-240 Light-brown crystals	$C_{16}H_{16}ClN_3$ C, 67.25; H, 5.64; N, 14.70; C, 67.11; H, 5.69; N, 14.48;	A
184		225-228 Light-brown crystals	$C_{16}H_{15}N_3O_2$ C, 68.31; H, 5.37; N, 14.94; C, 68.12; H, 5.40; N, 14.81;	A
185		211-212 Gray powder	$C_{13}H_{10}N_2O_2$ C, 69.02; H, 4.46; N, 12.38; C, 69.08; H, 4.55; N, 12.37;	I
186		212-213 Colorless crystals	$C_{15}H_{13}F_2N_3$ C, 65.93; H, 4.79; N, 15.38; C, 65.93; H, 4.68; N, 15.16;	A
187		206-207 Light-green crystals	$C_{15}H_{13}F_2N_3$ C, 65.93; H, 4.79; N, 15.38; C, 66.50; H, 4.92; N, 15.32;	A
188		260-268 Light-yellow needles	$C_{17}H_{15}N_3O$ C, 73.63; H, 5.45; N, 15.15; C, 73.68; H, 5.58; N, 14.14;	A

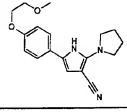
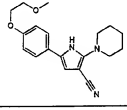
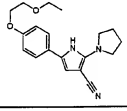
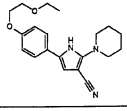
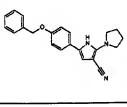
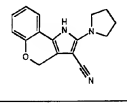
Continuation of Table 2

189		208-209 Light-yellow needles	$C_{14}H_{10}N_2O$ C, 75.66; H, 4.54; N, 12.60; C, 75.50; H, 4.78; N, 12.58;	I
190		201-203 Reddish brown powder	$C_{16}H_{16}N_4$ C, 72.15; H, 6.81; N, 21.04; C, 71.83; H, 6.98; N, 21.07;	A
191		160-161 Light-yellow crystals	$C_{16}H_{16}N_4$ C, 72.15; H, 6.81; N, 21.04; C, 72.11; H, 6.95; N, 20.93;	A
192		190-191 Purple crystals	$C_{10}H_{13}N_3$ C, 68.54; H, 7.48; N, 23.98; C, 68.55; H, 7.35; N, 24.09;	A
193		189-191 Purple crystals	$C_{11}H_{15}N_3$ C, 69.81; H, 7.99; N, 22.20; C, 69.64; H, 8.16; N, 21.92;	A
194		125-127 Colorless needles	$C_{13}H_{11}FN_2$ C, 72.88; H, 5.18; N, 13.08; C, 73.11; H, 5.39; N, 13.08;	I

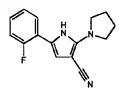
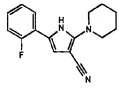
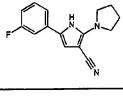
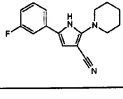
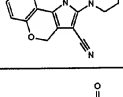
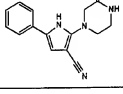
Continuation of Table 2

195		202-203 Colorless powder	$C_{20}H_{15}N_3O$ C, 76.66; H, 4.83; N, 13.41; C, 76.94; H, 4.94; N, 13.37;	I
196		196-198 Light-brown crystals	$C_{16}H_{16}N_4$ C, 72.15; H, 6.81; N, 21.04; C, 72.03; H, 6.88; N, 21.39;	A
197		156-158 Light-yellow crystals	$C_{14}H_{14}N_4$ C, 70.57; H, 5.92; N, 23.51; C, 70.72; H, 6.04; N, 23.58;	A
198		164-165 Purple crystals	$C_{12}H_{17}N_3$ C, 70.90; H, 8.43; N, 20.67; C, 70.56; H, 8.56; N, 20.67;	A
199		189-191 Light-brown crystals	$C_{16}H_{21}N_3O$ C, 73.19; H, 7.17; N, 14.23; C, 73.13; H, 7.42; N, 14.27;	A
200		204-206 Light-blue crystals	$C_{16}H_{23}N_3O$ C, 73.76; H, 7.49; N, 13.58; C, 73.72; H, 7.73; N, 13.63;	A

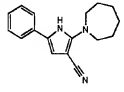
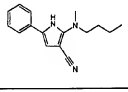
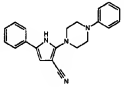
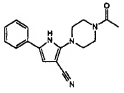
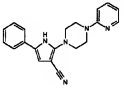
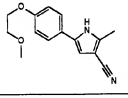
Continuation of Table 2

201		179-183 Light-green crystals	$C_{18}H_{21}N_3O_2$ C, 69.43; H, 6.80; N, 13.49; C, 69.48; H, 6.73; N, 13.56;	A
202		179-180 Colorless crystals	$C_{19}H_{23}N_3O_2$ C, 70.13; H, 7.12; N, 12.91; C, 70.01; H, 7.06; N, 12.84;	A
203		153-154 Light-brown crystals	$C_{19}H_{23}N_3O_2$ C, 70.13; H, 7.12; N, 12.91; C, 70.18; H, 7.15; N, 12.86;	A
204		172-174 Colorless crystals	$C_{20}H_{25}N_3O_2$ C, 70.77; H, 7.42; N, 12.38; C, 70.63; H, 7.36; N, 12.38;	A
205		211-213 Light-brown crystals	$C_{22}H_{21}N_3O$ C, 76.94; H, 6.16; N, 12.24; C, 76.83; H, 6.30; N, 12.22;	A
206		218-222 Light-brown crystals	$C_{16}H_{15}N_3O \cdot 1/10H_2O$ C, 71.94; H, 5.73; N, 15.73; C, 72.02; H, 5.77; N, 15.64;	A

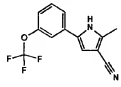
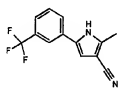
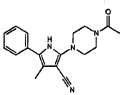
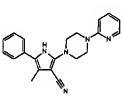
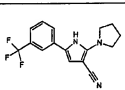
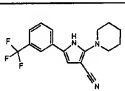
Continuation of Table 2

207		178-179 Light-yellow crystals	$C_{15}H_{14}FN_3$ C, 70.57; H, 5.53; N, 16.46; C, 70.65; H, 5.64; N, 16.44;	A
208		165-166 Blue crystals	$C_{16}H_{16}FN_3$ C, 71.36; H, 5.99; N, 15.60; C, 71.38; H, 6.14; N, 15.57;	A
209		220-221 Light-yellow crystals	$C_{15}H_{14}FN_3$ C, 70.57; H, 5.53; N, 16.46; C, 70.54; H, 5.65; N, 16.42;	A
210		182-183 Blue crystals	$C_{16}H_{16}FN_3$ C, 71.36; H, 5.99; N, 15.60; C, 71.56; H, 5.93; N, 15.65;	A
211		229-234 Light-brown crystals	$C_{17}H_{17}N_3O$ C, 73.10; H, 6.13; N, 15.04; C, 72.84; H, 6.12; N, 14.83;	A
212		263-265 White powder	$C_{15}H_{14}N_4O$ C, 67.65; H, 5.30; N, 21.04; C, 67.62; H, 5.29; N, 20.82;	A

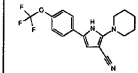
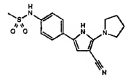
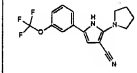
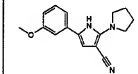
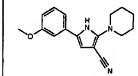
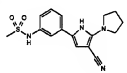
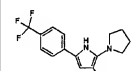
Continuation of Table 2

213		171-172 Light-brown crystals	$C_{17}H_{19}N_3$ C, 76.95; H, 7.22; N, 15.84; C, 76.87; H, 7.18; N, 15.74;	A
214		118-119 Blue plates	$C_{16}H_{19}N_3$ C, 75.85; H, 7.56; N, 16.59; C, 76.08; H, 7.17; N, 16.57;	A
215		238-239 Colorless crystals	$C_{21}H_{20}N_4$ C, 76.80; H, 6.14; N, 17.06; C, 77.07; H, 6.27; N, 17.08;	A
216		205-206 Light-yellow crystals	$C_{17}H_{18}N_4O$ C, 69.37; H, 6.16; N, 19.03; C, 69.41; H, 6.52; N, 19.06;	A
217		177-178 Colorless crystals	$C_{20}H_{19}N_5$ C, 72.92; H, 5.81; N, 21.26; C, 73.23; H, 6.04; N, 21.21;	A
218		163-164 Gray powder	$C_{15}H_{16}N_2O_2$ C, 70.29; H, 6.29; N, 10.93; C, 70.19; H, 6.28; N, 10.95;	I

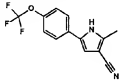
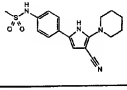
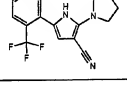
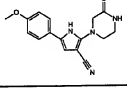
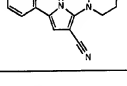
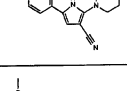
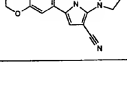
Continuation of Table 2

219		172-173 Colorless needles	$C_{13}H_9F_3N_2O$ C, 58.65; H, 3.41; N, 10.52; C, 58.88; H, 3.23; N, 10.63;	I
220		201-202 Colorless needles	$C_{13}H_9F_3N_2$ C, 62.40; H, 3.63; N, 11.20; C, 62.37; H, 3.74; N, 11.23;	I
221		190-192 Light-yellow crystals	$C_{18}H_{20}N_4O$ C, 70.11; H, 6.54; N, 18.17; C, 70.88; H, 6.44; N, 18.14;	A
222		215-216 Light-orange crystals	$C_{21}H_{21}N_5$ C, 73.44; H, 6.16; N, 20.39; C, 73.95; H, 6.24; N, 20.34;	A
223		259-263 Colorless crystals	$C_{16}H_{14}F_3N_3$ C, 62.95; H, 4.62; N, 13.76; C, 63.01; H, 5.16; N, 13.73;	A
224		207-208 Light-gray crystals	$C_{17}H_{16}F_3N_3$ C, 63.94; H, 5.05; N, 13.16; C, 64.61; H, 4.83; N, 13.08;	A

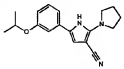
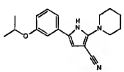
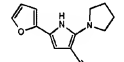
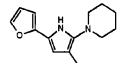
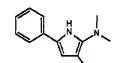
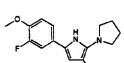
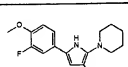
Continuation of Table 2

225		232-233 Light-brown crystals	$C_{17}H_{16}F_3N_3O$ C, 60.89; H, 4.81; N, 12.53; C, 60.88; H, 4.92; N, 12.29;	A
226		252-260 Brown crystals	$C_{16}H_{18}N_4O_2S$ C, 58.16; H, 5.49; N, 16.96; C, 57.92; H, 5.46; N, 16.84;	A
227		225-228 Light-yellow crystals	$C_{16}H_{14}F_3N_3O$ C, 59.81; H, 4.39; N, 13.08; C, 60.06; H, 4.58; N, 13.08;	A
228		198-200 Light-brown crystals	$C_{16}H_{17}N_3O$ C, 71.89; H, 6.41; N, 15.72; C, 72.02; H, 6.37; N, 15.77;	A
229		172-174 Light-yellow crystals	$C_{17}H_{19}N_3O$ C, 72.57; H, 6.81; N, 14.94; C, 72.60; H, 6.78; N, 14.51;	A
230		210-216 Light-brown crystals	$C_{16}H_{18}N_4O_2S$ C, 58.16; H, 5.49; N, 16.96; C, 58.06; H, 5.64; N, 16.82;	A
231		274-281 Light-yellow crystals	$C_{16}H_{14}F_3N_3$ C, 62.95; H, 4.62; N, 13.76; C, 63.19; H, 4.61; N, 13.66;	A

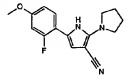
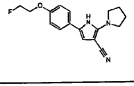
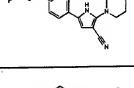
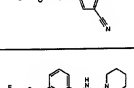
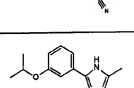
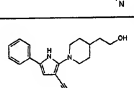
Continuation of Table 2

232		167-168 Colorless needles	$C_{13}H_8F_3N_2O \cdot 1/10C_6H_6$ C, 59.61; H, 3.53; N, 10.22; C, 59.54; H, 3.27; N, 10.43;	I
233		245-248 Gray crystals	$C_{17}H_{20}N_4O_2S \cdot C_2H_5OH$ C, 58.44; H, 6.71; N, 14.35; C, 58.28; H, 6.42; N, 14.58;	A
234		216-217 Colorless crystals	$C_{16}H_{14}F_3N_3$ C, 62.95; H, 4.62; N, 13.76; C, 63.16; H, 4.38; N, 13.76;	A
235		273-278 Light-brown powder	$C_{16}H_{15}N_4O_2$ C, 64.85; H, 5.44; N, 18.91; C, 64.91; H, 5.22; N, 18.99;	A
236		213-214 Light-blue crystals	$C_{15}H_{15}N_3S$ C, 66.88; H, 5.61; N, 15.60; C, 66.81; H, 5.63; N, 15.54;	A
237		252-253 Colorless crystals	$C_{16}H_{17}N_3OS$ C, 64.19; H, 5.72; N, 14.04; C, 64.18; H, 5.76; N, 14.08;	A
238		155-157 Light-brown powder	$C_{16}H_{21}N_3O_2$ C, 69.43; H, 6.80; N, 13.49; C, 69.29; H, 6.67; N, 13.46;	A

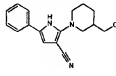
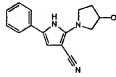
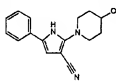
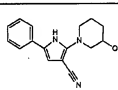
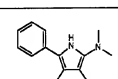
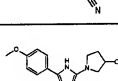
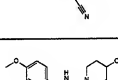
Continuation of Table 2

239		295-298 Light-brown powder.	$C_{18}H_{21}N_3O$ C, 73.19; H, 7.17; N, 14.23; C, 72.94; H, 6.92; N, 13.92;	A
240		163-164 Light-green crystals	$C_{19}H_{23}N_3O$ C, 73.76; H, 7.49; N, 13.58; C, 73.80; H, 7.60; N, 13.58;	A
241		196-199 Yellowish green crystals	$C_{13}H_{13}N_3O$ C, 68.70; H, 5.77; N, 18.49; C, 68.29; H, 5.55; N, 18.33;	A
242		158-161 Deep-green crystals	$C_{14}H_{15}N_3O \cdot 3/10H_2O$ C, 68.16; H, 6.37; N, 17.03; C, 67.98; H, 5.97; N, 17.00;	A
243		175-176 Light-brown crystals	$C_{13}H_{13}N_3$ C, 73.91; H, 6.20; N, 19.89; C, 73.81; H, 6.21; N, 19.77;	A
244		238-245 Colorless powder	$C_{18}H_{16}FN_3O$ C, 67.35; H, 5.65; N, 14.73; C, 67.42; H, 5.74; N, 14.53;	A
245		211-212 Blue crystals	$C_{17}H_{18}FN_3O$ C, 68.21; H, 6.06; N, 14.04; C, 68.20; H, 6.21; N, 13.73;	A

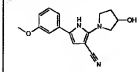
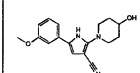
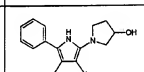
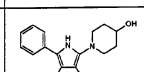
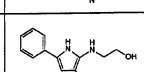
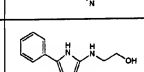
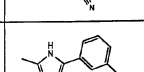
Continuation of Table 2

246		222-224 Light-brown crystals	$C_{16}H_{16}FN_3O$ C, 67.35; H, 5.65; N, 14.73; C, 67.54; H, 5.88; N, 14.66;	A
247		203-206 Light-brown crystals	$C_{17}H_{18}FN_3O$ C, 68.21; H, 6.06; N, 14.04; C, 68.38; H, 6.11; N, 13.98;	A
248		207-209 Light-brown crystals	$C_{18}H_{20}FN_3O$ C, 68.99; H, 6.43; N, 13.41; C, 69.01; H, 6.39; N, 13.32;	A
249		169-171 Light-yellow crystals	$C_{17}H_{18}FN_3O$ C, 68.21; H, 6.06; N, 14.04; C, 68.34; H, 6.12; N, 13.93;	A
250		142-144 Light-purple crystals	$C_{18}H_{20}FN_3O$ C, 68.99; H, 6.43; N, 13.41; C, 69.23; H, 6.41; N, 13.31;	A
251		131-132 Light-red powder	$C_{15}H_{16}N_2O$ C, 74.97; H, 6.71; N, 11.66; C, 75.07; H, 6.75; N, 11.55;	I
252		173-174 Colorless crystals	$C_{18}H_{21}N_3O$ C, 73.19; H, 7.17; N, 14.23; C, 73.08; H, 7.41; N, 14.18;	A

Continuation of Table 2

253		133-134 Light-purple crystals	$C_{17}H_{19}N_3O$ C, 72.57; H, 6.81; N, 14.94; C, 72.58; H, 6.88; N, 14.95;	A
254		167-168 Light-yellow crystals	$C_{15}H_{15}N_3O$ C, 71.13; H, 5.97; N, 16.59; C, 71.09; H, 6.06; N, 16.66;	A
255		176-177 Blue crystals	$C_{16}H_{17}N_3O$ C, 71.89; H, 6.41; N, 15.72; C, 71.75; H, 6.50; N, 15.76;	A
256		171-172 Purple crystals	$C_{16}H_{17}N_3O$ C, 71.89; H, 6.41; N, 15.72; C, 71.93; H, 6.67; N, 15.71;	A
257		189-191 Bluish green crystals	$C_{14}H_{15}N_3$ C, 74.64; H, 6.71; N, 18.65; C, 75.09; H, 6.77; N, 18.64;	A
258		225-230 Colorless crystals	$C_{16}H_{17}N_3O_2$ C, 67.83; H, 6.05; N, 14.83; C, 68.00; H, 6.29; N, 14.83;	A
259		216-217 Colorless crystals	$C_{17}H_{19}N_3O_2$ C, 68.67; H, 6.44; N, 14.13; C, 68.80; H, 6.66; N, 14.14;	A

Continuation of Table 2

260		133-135 Colorless crystals	$C_{16}H_{17}N_3O_2$ C, 67.83; H, 6.05; N, 14.83; C, 67.87; H, 6.27; N, 14.81;	A
261		179-181 Light-brown crystals	$C_{17}H_{19}N_3O_2$ C, 68.67; H, 6.44; N, 14.13; C, 68.43; H, 6.44; N, 13.86;	A
262		200-201 Light-pink crystals	$C_{16}H_{17}N_3O$ C, 71.89; H, 6.41; N, 15.72; C, 71.81; H, 6.40; N, 15.52;	A
263		202-204 Light-blue crystals	$C_{17}H_{19}N_3O$ C, 72.57; H, 6.81; N, 14.94; C, 72.37; H, 6.79; N, 14.57;	A
264		150-151 Colorless crystals	$C_{13}H_{13}N_3O$ C, 68.70; H, 5.77; N, 18.49; C, 68.63; H, 5.81; N, 18.34;	A
265		143-144 Colorless crystals	$C_{14}H_{15}N_3O$ C, 69.69; H, 6.27; N, 17.41; C, 69.57; H, 6.26; N, 17.33;	A
266		212-213 Colorless powder	$C_{13}H_9N_3$ C, 75.35; H, 4.38; N, 20.28; C, 75.34; H, 4.47; N, 20.08;	H

Test Examples

The following are the results of pharmacological tests of some representative species, which demonstrate the usefulness of the compound of the invention.

Test Example 1

Cystometrography (rats)

Cystometrography is a method for ascertaining the relation between intravesical pressure and bladder capacity and provides information on the time course of condition of the urinary bladder from urine filling to micturition, the possible involuntary contraction of the urinary bladder, and the contractility of the detrusor muscle during micturition.

The experiment was performed using 9 to 13-weeks old female SD rats in groups of 3-5. After a median incision was made in the abdominal region under urethane anesthesia, a polyethylene indwelling cannula was inserted into the urinary bladder dome through the apex of the urinary bladder and fixed. The other end of the cannula was connected to a T-tube for infusion of saline via one branch and changes in intravesical pressure were recorded via the other branch. When warmed saline was continuously infused into the urinary bladder at a constant rate, the urinary bladder was distended and, when the pressure reached a threshold, the urinary bladder underwent rapid contractions and at the same time a micturition was induced. This procedure was repeated until the volume of saline from the start of infusion to the threshold intravesical pressure (bladder capacity) became steady giving approximately constant values in at least two consecutive determinations. Then, the test compound was administered into the duodenum. The bladder capacity was measured immediately before administration of the test compound and 0.5, 1, 2, and 3 hours after administration. The maximum increase rate (%) in bladder capacity was calculated by means of the following equation.

$$\text{Maximum increase rate in bladder capacity} = [(A-B)/B] \times 100$$

where B represents the bladder capacity value immediately before administration of the test compound and A represents the maximum bladder capacity at 0.5, 1, 2, and 3 hours after administration of the test compound. Results of the test are shown in Table 3. The data shown are mean values.

Table 3

Cystometrography (rats)		
Compound No.	Dosage (mg/kg)	Maximum increase rate (%) in bladder capacity
R1	3	63.6
1	3	60.8
8	30	55.4
15	10	53.8
41	10	38.8
63	3	49.9
Propiverine	100	42.0
(Compound No. corresponds to that in Table 1 or 2)		

The compounds of the invention produced equivalent or more potant effect in the increase of bladder capacity at markedly lower dose levels as compared with the reference prior art drug.

It is clear from the above results that the compounds of the invention have potent bladder capacity increasing activity.

Test Example 2

Acute toxicity test

Male ddY mice, 6 to 7-weeks old, were used in groups of 4-5. The animals fasted from the previous day (16-18 hours before the experiment) were given the test compound by oral gavage using a gastric tube and monitored for death for 2 weeks. As shown in Table 4, no death was encountered at all, nor was observed any abnormal finding.

Table 4

Acute toxicity test in mice		
Compound No.	Dosage (mg/kg)	Dead/Total
R1	1000	0/4
1	1000	0/4
8	1000	0/4
41	1000	0/5
63	1000	0/5

Formulation Example 1

Tablets (oral dosage form)

In 200 mg per tablet:

Compound No. R1	20 mg
Corn starch	88 mg
Crystalline cellulose	80 mg
Carboxymethylcellulose calcium	10 mg
Light silicic anhydride	1 mg
Magnesium stearate	1 mg

A powdery mixture of the above composition was compressed to provide oral tablets.

Formulation Example 2

Tablets (oral dosage form)

In 200 mg per tablet

Compound No. 1	20 mg
Corn starch	88 mg
Crystalline cellulose	80 mg
Carboxymethylcellulose calcium	10 mg
Light silicic anhydride	1 mg
Magnesium stearate	1 mg

A powdery mixture of the above composition was compressed to provide oral tablets. Formulation Example 3

Tablets (oral dosage form)

In 200 mg per tablet:

Compound No. 63	20 mg
Corn starch	88 mg
Crystalline cellulose	80 mg
Carboxymethylcellulose calcium	10 mg
Light silicic anhydride	1 mg
Magnesium stearate	1 mg

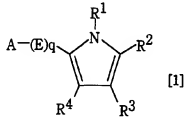
A powdery mixture of the above composition was compressed to provide oral tablets.

INDUSTRIAL APPLICABILITY

As described above, the compound of the present invention has potent bladder capacity increasing activity with a low toxic potential and is, therefore, useful for the treatment of pollakiuria or urinary incontinence.

Claims

1. (after amendment) A pharmaceutical composition for the treatment of pollakiuria or urinary incontinence which comprises a pyrrole derivative of the following formula [1] or a pharmaceutically acceptable salt thereof, or a solvate of either of them, as an active ingredient.

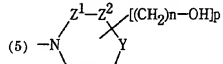


[1]

wherein R^1 represents hydrogen or alkoxycarbonylamino;
R^2 represents (1) alkyl, (2) aryl which may be substituted, (3) aromatic heterocyclyl which may be substituted,

(4)

or



(5)

;

R^6 and R^7 may be the same or different and each represents (1) hydrogen or (2) alkyl (which alkyl may be substituted by (1) hydroxy, (2) aryl which may be substituted by alkoxy, or (3) aromatic heterocyclyl);
Z^1 and Z^2 may be the same or different and each represents $-CH_2-$ or >C=O; provided that Z^1 and Z^2 do not concurrently represent >C=O;
Y represents $-CH_2-$, -O-, -S-, or $>NR^9$;
R^9 represents hydrogen, alkyl, acyl, aryl, or aromatic heterocyclyl;
m represents an integer of 1-3; n represents an integer of 0-2; p represents 0 or 1;
in case R^2 represents aryl which may be substituted or aromatic heterocyclyl which may be substituted, the

aryl or aromatic heterocyclyl may be substituted by 1 member or 2-3 different members selected from the group consisting of (1) halogen, (2) alkyl which maybe substituted by halogen, (3) cyano, (4) nitro, (5) alkoxycarbonyl, (6) hydroxy, (7) alkoxy (which alkoxy may be substituted by halogen, aryl which may be substituted by alkoxy, or alkoxy), (8) $-NHSO_2R^{92}$, and (9) $-NR^{93}R^{94}$; or two adjacent substituent groups may jointly represent $-O-(CH_2)_t-O-$,

R^{92} represents (1) alkyl or (2) aryl which may be substituted by alkyl;

t represents 1 or 2;

R^{93} and R^{94} may be the same or different and each represents (1) hydrogen, (2) alkyl, or (3) acyl; or R^{93} and R^{94} jointly and taken together with the adjacent N atom represent 5-through 7-membered cyclic amino;

R^3 represents cyano or carbamoyl;

R^4 represents hydrogen or alkyl;

E represents alkylene; q represents 0 or 1;

A represents (1) methyl, (2) aryl which may be substituted, or (3) aromatic heterocyclyl which may be substituted;

in case A represents aryl which may be substituted or aromatic heterocyclyl which may be substituted, the aryl or aromatic heterocyclyl may be substituted by 1 member or 2-3 different members selected from the group consisting of (1) halogen, (2) alkyl which may be substituted by halogen, (3) cyano, (4) nitro, (5) alkoxycarbonyl, (6) hydroxy, (7) alkoxy (which alkoxy may be substituted by halogen, aryl which may be substituted by alkoxy, or alkoxy), (8) $-NHSO_2R^{92}$, and (9) $-NR^{93}R^{94}$; or two adjacent substituent groups may jointly represent $-O-(CH_2)_u-O-$;

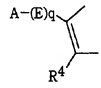
R^{92} represents (1) alkyl or (2) aryl which may be substituted by alkyl;

u represents 1 or 2;

R^{93} and R^{94} may be the same or different and each represents (1) hydrogen, (2) alkyl, or (3) acyl; or R^{93} and R^{94} jointly and taken together with the adjacent N atom represent 5-through 7-membered cyclic amino;

A-(E)q, R^4, and the double bond of the pyrrole ring may jointly, i.e.

as



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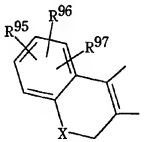


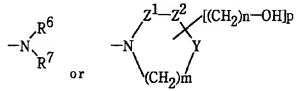
;

X represents -O-, -S-, or $>NR^{90}$ where R^{90} represents alkyl;

R^{95}, R^{96} and R^{97} may be the same or different and each is selected from the group consisting of (1) hydrogen, (2) halogen, (3) alkyl which may be substituted by halogen, (4) cyano, (5) nitro, (6) alkoxycarbonyl, (7) hydroxy, (8) alkoxy (which alkoxy may be substituted by halogen or alkoxy), (9) $-NHSO_2R^{92}$ (R^{92} is as defined above), and (10) $-NR^{93}R^{94}$ (R^{93} and R^{94} are as defined above); any two adjacent substituent groups among R^{95}, R^{96}, and R^{97} may jointly represent $-O-(CH_2)_u-O-$ (u is as defined above).

2. (after amendment) A pharmaceutical composition for the treatment of pollakiuria or urinary incontinence which

comprises a pyrrole derivative, a pharmaceutically acceptable salt, or a solvate of either of them described in Claim 1 as an active ingredient, wherein R^2 represents



3. A pharmaceutical composition for the treatment of pollakiuria or urinary incontinence which comprises a pyrrole derivative, a pharmaceutically acceptable salt, or a solvate of either of them described in Claim 1 or 2 as an active ingredient.

4. A pharmaceutical composition for the treatment of pollakiuria or urinary incontinence which comprises a pyrrole derivative, a pharmaceutically acceptable salt, or a solvate of either of them described in Claim 1 wherein R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is hydrogen or alkyl, q is equal to 0, and A is (1) aryl which may be substituted or (2) aromatic heterocyclyl which may be substituted as an active ingredient.

5. A pharmaceutical composition for the treatment of pollakiuria or urinary incontinence which comprises a pyrrole derivative, a pharmaceutically acceptable salt, or a solvate of either of them described in Claim 1 or Claim 2 wherein R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is methyl, q is equal to 0, and A is phenyl, 2-fluorophenyl, 2,5-difluorophenyl, or 3-pyridyl as an active ingredient.

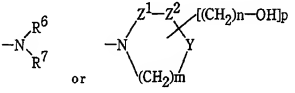
6. A pharmaceutical composition for the treatment of pollakiuria or urinary incontinence which comprises a pyrrole derivative, a pharmaceutically acceptable salt, or a solvate of either of them described in Claim 1 wherein R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is phenyl or 4-fluorophenyl as an active ingredient.

7. (after amendment) A pyrrole derivative, a pharmaceutically acceptable salt, or a solvent of either of them described in Claim 1 excluding the following cases:

(1) R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is methyl, q is equal to 0, and A is methyl, phenyl, or 4-hydroxyphenyl,
(2) R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is methyl, -(E)q- is $-CH_2-$, and A is methyl, phenyl, 4-hydroxyphenyl, 4-chlorophenyl, or 3-indolyl,
(3) R^1 is hydrogen, R^2 is morpholino, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is methyl or phenyl,
(4) R^1 is hydrogen, R^2 is 1-pyrrolidinyl, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is phenyl, 4-bromophenyl, 4-nitrophenyl, or 2,4-dimethylphenyl,
(5) R^1 is hydrogen, R^2 is 1-piperidinyl, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is phenyl or 4-bromophenyl,
(6) R^1 is hydrogen, R^2 is diethylamino, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is methyl, phenyl, 4-bromophenyl, or 3-nitrophenyl,
(7) R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is methyl, -(E)q- is $-CH_2CH_2-$, and A is methyl,
(8) R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is n-propyl, -(E)q- is $-CH_2-$, and A is methyl,
(9) R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is methyl, -(E)q- is $-CH(CH_3)CH_2-$, and A is methyl,
(10) R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is ethyl, q is equal to 0, and A is methyl,
(11) R^1 is hydrogen, R^2 is methylamino, R^3 is cyano, R^4 is methyl, q is equal to 0, and A is methyl,
(12) R^1 is hydrogen, R^2 is 2-oxopyrrolidin-1-yl, R^3 is cyano, R^4 is methyl, q is equal to 0, and A is methyl,
(13) R^1 is hydrogen, R^2 is 1-piperidinyl, R^3 is cyano, R^4 is methyl, q is equal to 0, and A is phenyl,
(14) R^1 is hydrogen, R^2 is n-butylamino, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is phenyl,
(15) R^1 is hydrogen, R^2 is methyl, R^3 is cyano, R^4 is methyl, q is equal to 0, and A is methyl or phenyl,
(16) R^1 is hydrogen, R^2 is methyl, R^3 is carbamoyl, R^4 is methyl, q is equal to 0, and A is methyl,
(17) R^1 is hydrogen, R^2 is methyl, R^3 is carbamoyl, R^4 is hydrogen, q is equal to 0, and A is methyl or phenyl,
(18) R^1 is hydrogen, R^2 is methyl, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is methyl or phenyl,

(19) R^1 is hydrogen, R^2 is methyl, R^3 is cyano, R^4 is hydrogen, -(E)q- is $-CH(CH_3)CH_2-$, and A is methyl,
(20) R^1 is hydrogen, R^2 is phenyl, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is methyl or phenyl,
(21) R^1 is hydrogen, R^2 is isobutyl, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is methyl,
(22) R^1 is hydrogen, R^2 is 4-methoxycarbonylphenyl, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is methyl,
(23) R^1 is hydrogen, R^2 is 4-methoxycarbonylphenyl, R^3 is cyano, R^4 is hydrogen, -(E)q- is $-CH_2-$, and A is methyl,
(24) R^1 is hydrogen, R^2 is 2-thienyl, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is 2-thienyl or 2-furanyl,
(25) R^1 is hydrogen, R^2 is 4-nitrophenyl, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is phenyl,
(26) R^1 is hydrogen, R^2 is 1-isoquinolinyl, R^3 is cyano or carbamoyl, R^4 is hydrogen, q is equal to 0, and A is phenyl,
(27) R^1 is hydrogen, R^2 is 2-furanyl, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is 2-thienyl or 2-furanyl,
(28) R^1 is hydrogen, R^2 is methyl, R^3 is cyano, R^4 is methyl, -(E)q- is $-CH_2-$, and A is methyl,
(29) R^1 is hydrogen, R^2 is 5-nitrobenzimidazol-1-yl, R^3 is cyano, R^4 is methyl, q is equal to 0, and A is methyl,
(30) R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is methyl, -(E)q- is $-CH_2-$, and A is 4-methoxyphenyl or 1-methyl-3-indolyl.

8. (after amendment) A pyrrole derivative, a pharmaceutically acceptable salt, or a solvate of either of them described in Claim 7 wherein R^2 is



or

.

9. A pyrrole derivative, a pharmaceutically acceptable salt, or a solvate of either of them described in Claim 7 wherein R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is hydrogen or alkyl, q is equal to 0, and A is (1) aryl which may be substituted or (2) aromatic heterocyclyl which may be substituted.

10. A pyrrole derivative, a pharmaceutically acceptable salt, or a solvate of either of them described in Claim 7 wherein R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is methyl, q is equal to 0, and A is 2-fluorophenyl, 2,5-difluorophenyl, or 3-pyridyl.

11. A pyrrole derivative, a pharmaceutically acceptable salt, or a solvate of either of them described in Claim 7 wherein R^1 is hydrogen, R^2 is NH_2, R^3 is cyano, R^4 is hydrogen, q is equal to 0, and A is phenyl or 4-fluorophenyl.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP96/01526

A. CLASSIFICATION OF SUBJECT MATTER Int. Cl[6] C07D207/335, 207/34, 401/04, 401/14, 403/04, 405/04, 405/14, 409/04, 413/04, 417/04, 491/52, A61K31/40, 31/44, 31/445, 31/495, 31/535, 31/54, 31/55
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) Int. Cl[6] C07D207/335, 207/34, 401/04, 401/14, 403/04, 405/04, 405/14, 409/04, 413/04, 417/04, 491/52, A61K31/40, 31/44, 317445, 31/495, 31/535, 31/54, 31/55

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CAS ONLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	WO, 93/19067, A1 (Fujisawa Pharmaceutical Co., Ltd.), September 30, 1993 (30. 09. 93), Full descriptions & JP, 7-508260, A	1 2 - 11
X A	JP, 4-288075, A (Fujisawa Pharmaceutical Co., Ltd.), October 13, 1992 (13. 10. 92), Full descriptions & EP, 480204, A & NO, 9103750, A & AU, 9183454, A & CA, 2052125, A & FI, 9104163, A & HU, 59404, A & ZA, 9107228, A & CN, 1059723, A & PT, 99038, A & US, 5210092, A & US, 5215994, A	1 2 - 11
X A	JP, 2-292327, A (Miles Inc.), December 3, 1990 (03. 12. 90), Full descriptions & EP, 389904, A & AU, 9052357, A & CA, 2010170, A & US, 5021586, A & US, 5068355, A	1, 7 2-6, 8-11

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
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Date of the actual completion of the international search	Date of mailing of the international search report
September 24, 1996 (24. 09. 96)	October 8, 1996 (08. 10. 96)
Name and mailing address of the ISA/ Japanese Patent Office Facsimile No.	Authorized officer Telephone No.

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International application No.
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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X A	DD, 143426, A (Ger. Dem. Rep.), August 20, 1980 (20. 08. 80), Full descriptions (Family: none)	1 2 - 11
P,X P,A	J. Heterocycl. Chem., 33(1), (1996), p. 161-8, Girolamo Cirrincione et al., "Reactivity of aminopyrroles: Protonation(a)	1, 2 3 - 11
X A	J. Chem. Res., Synop., (8), (1992), p. 266-7, Sze-Ming Lee et al., "The synthesis and chemistry of azolenines. Part 22. Alternative pathways in the reaction between 1-chloroalkylidenemalononitriles and 2-methyl-3-phenyl-2H-azirine"	1 2 - 11
X A	Egypt. J. Pharm. Sci., 32(1-2), (1991), p. 303-14, N. G. Hares et al., "Synthesis and antibacterial activity of some 4-oxopyrrolo (1,2-a)pyrimidine 3-caarboxylic acid derivatives"	1, 2 3 - 11
X A	J. Indian. Chem. Soc., 68(7), (1991), p. 396-7, Chaitanya G. Dave et al., "Study of reaction between 2-amino-3-cyanopyrroles and isothiocyanates. Synthesis of 4-aminopyrrolo (2,3-d)-pyrimidine-2(3H)-thiones"	1, 2 3 - 11

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP96/01526

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	Indian J. Chem., Sect. B. 27B(8), (1988), p. 778-80, Chaitanya G. Dave et al., "Synthesis & biological activity of pyrrolo(2,3-d) pyrimidines"	1 2 - 11
X A	Farmaco, Ed. Sci., 43(1), (1988), p. 103-12, M. T. Cocco et al., "Synthesis and biological activity of some pyrrole derivatives"	1, 2 3 - 11
X A	J. Heterocycl. Chem., 23(2), (1986), p. 397-400, Werner Zimmermann et al., "Synthesis of substituted pyrrolo(1,2-a)(1,3)diazepine. A correction"	1, 7 2-6, 8-11
X A	Arch. Pharm. (Weinheim, Ger.), 318(10), (1985), p. 953-4, Gerd Folkers et al., "Ein Weg zu N-1-heterocyclisch substituierten 5-Nitrobenzimidazolen"	1, 7 2-6, 8-11
X A	Liebigs Ann. Chem., (12), (1983), p. 2066-72, Nabih S. Giegis et al., "Synthesis of 3-aryl-3,7-dihydro-4H-pyrrolo(2,3-d)pyrimidin-4-imines"	1 2 - 11
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X A	J. Pharm. Sci., 70(2), (1981), p. 135-40, J. Walter Sowell et al., "Synthesis of alkylaminoalkylamides of substituted 2-aminopyrroles as potential local anesthetic and antiarrhythmic agents I:α-amines"	1, 2 3 - 11
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X A	J. Pharm. Sci., 69(4), (1980), p. 473-5, Debra L. Powers et al., "Anticonvulsant Properties of selected pyrrolo(2,3-d)pyrimidine-2,4-diones and intermediates"	1, 2 3 - 11
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X A	Heterocycles, 10, (1978), p. 261-4, Tetsuo Kato et al., "Reaction of β-amino-crotonamides with α-haloketones and α-hydroxyketones"	1 2 - 11
X A	Synthesis, (3), (1979), p. 217-8, Ronald J. Mattson et al., "Selective N-1-methylation of	1, 7 2-6, 8-11

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP96/01526

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	2-aminopyrroles with sodium hydride and dimethyl sulfate"	
X A	J. Pharm. Sci., 68(3), (1979), p. 317-20, Ronald W. Johnson et al., "Synthesis of substituted 2-aminopyrrole analogs of lidocaine I"	1, 2 3 - 11
X A	J. Org. Chem., 43(22), (1978), p. 4273-6, Isabel A. Benages et al., "2-Chloroacrylonitrile as a cyclodipolarophile in 1,3-cycloadditions. 3-cyanopyrroles"	1 2 - 11
X A	J. Heterocycl. Chem., 14(3), (1977), p. 383-5, Ronald W. Johnson et al., "Synthesis of substituted 2-amino-3-cyano-4-methylpyrroles"	1, 2 3 - 11
X A	Khim. Geterotsikl, Soedin., (12), (1976), p. 1677-81, Shvedov V.I. et al., "Synthesis of pyrrolo(1,2-a)pyrimidine derivatives"	1 2 - 11
X A	J. Prakt. Chem., 318(4), (1976), p. 663-70, Von K. Gewald et al., "Reaction of .alpha. -cyano-.gamma.-halocrotononitriles with amines"	1 2 - 11
X A	Khim. Geterotsikl. Soedin., (9), (1975), p. 1217-24, Shvedov V. I. et al., "Synthesis of substituted 2-amino-3-cyanopyrroles"	1 2 - 11
X A	Synthesis, (1), (1974), p. 55-6, Roy A. Crochet, Jr. et al., "N-monoalkylation of primary aromatic amines with trialkyl orthocarboxylates and sodium borohydrate"	1 2 - 11
X A	Chem. Ber., 105(4), (1972), p. 1258-78, Rolf Huisgen et al., "1,3-Dipolar cyclo-additions. 62. Benzonitrile 4-nitrobenzylide and its reactions with carbon-carbon double and triple bonds"	1 2 - 11
X A	J. Chem. Soc. B, (1), (1970), p. 79-81, L. F. Elsom et al., "Pyrrole Studies. Part XIV. Spectroscopic characteristics of cyanopyrroles"	1 2 - 11
X A	J. Org. Chem., 31(12), (1966), p. 4110-18, Eleftheria K. Evanguelidou et al., "Acid-catalyzed condensation of a Resisert compound with acrylonitrile"	1 2 - 11

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